10/789,063

EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	2750	((514/343) or (514/310) or (514/313)).CCLS.	US-PGPUB; USPAT; USOCR	OR	OFF	2007/07/19 16:50
L2	3013	((546/256) or (546/143) or (546/159)).CCLS.	US-PGPUB; USPAT; USOCR	OR	OFF	2007/07/19 16:50
L3	4683	L1 or L2	US-PGPUB; USPAT	OR	OFF	2007/07/19 16:51
L4	789	L3 and (pyrrolid$4 with amino)	US-PGPUB; USPAT	OR	OFF	2007/07/19 16:55

10/789,063

EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	3409	((514/422) or (514/424) or (514/426)).CCLS.	US-PGPUB; USPAT; USOCR	OR	OFF	2007/07/10 11:05
L2	2040	((548/518) or (548/543) or (548/558)).CCLS.	US-PGPUB; USPAT; USOCR	OR	OFF	2007/07/10 11:06
L3	4567	L1 or L2	US-PGPUB; USPAT	OR	OFF	2007/07/10 11:06
L4	3084	L3 and pyrrolid$4	US-PGPUB; USPAT	OR	OFF	2007/07/10 11:07
L5	538	L4 and ('3-hydroxy' or '3-oxo' or pyrrolidinone)	US-PGPUB; USPAT	OR	OFF	2007/07/10 11:08

10/ 789,063

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:ssspta1202txn

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page for STN Seminar Schedule - N. America
NEWS 2	MAR 15	WPIDS/WPIX enhanced with new FRAGHITSTR display format
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NEWS 4	MAR 20	MARPAT now updated daily
NEWS 5	MAR 22	LWPI reloaded
NEWS 6	MAR 30	RDISCLOSURE reloaded with enhancements
NEWS 7	APR 02	JICST-EPLUS removed from database clusters and STN
NEWS 8	APR 30	GENBANK reloaded and enhanced with Genome Project ID field
NEWS 9	APR 30	CHEMCATS enhanced with 1.2 million new records
NEWS 10	APR 30	CA/CAplus enhanced with 1870-1889 U.S. patent records
NEWS 11	APR 30	INPADOC replaced by INPADOCDB on STN
NEWS 12	MAY 01	New CAS web site launched
NEWS 13	MAY 08	CA/CAplus Indian patent publication number format defined
NEWS 14	MAY 14	RDISCLOSURE on STN Easy enhanced with new search and display fields
NEWS 15	MAY 21	BIOSIS reloaded and enhanced with archival data
NEWS 16	MAY 21	TOXCENTER enhanced with BIOSIS reload
NEWS 17	MAY 21	CA/CAplus enhanced with additional kind codes for German patents
NEWS 18	MAY 22	CA/CAplus enhanced with IPC reclassification in Japanese patents
NEWS 19	JUN 27	CA/CAplus enhanced with pre-1967 CAS Registry Numbers
NEWS 20	JUN 29	STN Viewer now available
NEWS 21	JUN 29	STN Express, Version 8.2, now available
NEWS 22	JUL 02	LEMBASE coverage updated
NEWS 23	JUL 02	LMEDLINE coverage updated
NEWS 24	JUL 02	SCISEARCH enhanced with complete author names
NEWS 25	JUL 02	CHEMCATS accession numbers revised
NEWS 26	JUL 02	CA/CAplus enhanced with utility model patents from China

NEWS EXPRESS 29 JUNE 2007: CURRENT WINDOWS VERSION IS V8.2,
CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
AND CURRENT DISCOVER FILE IS DATED 4 MAY 2007.

NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS LOGIN	Welcome Banner and News Items
NEWS IPC8	For general information regarding STN implementation of IPC 8

Enter NEWS followed by the item number or name to see news on that specific topic.

result in loss of user privileges and other penalties.

* * * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 14:09:22 ON 02 JUL 2007

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 14:09:33 ON 02 JUL 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 1 JUL 2007 HIGHEST RN 940612-32-8
DICTIONARY FILE UPDATES: 1 JUL 2007 HIGHEST RN 940612-32-8

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TSCA INFORMATION NOW CURRENT THROUGH December 2, 2006

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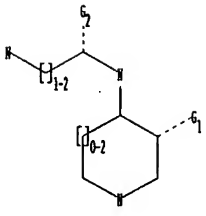
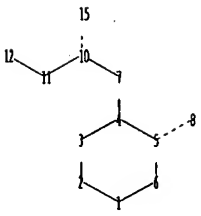
REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=>
Uploading C:\Program Files\Stnexp\Queries\10789063.str





chain nodes :
7 8 10 11 12 15
ring nodes :
1 2 3 4 5 6
chain bonds :
4-7 5-8 7-10 10-11 10-15 11-12
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6
exact/norm bonds :
4-7 5-8 7-10 10-15 11-12
exact bonds :
1-2 1-6 2-3 3-4 4-5 5-6 10-11
isolated ring systems :
containing 1 :

G1:O,OH

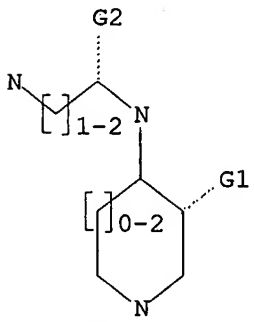
G2:H,O

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 10:CLASS
11:CLASS 12:CLASS 15:CLASS

L1 STRUCTURE UPLOADED

=> d L1

L1 HAS NO ANSWERS
L1 STR



G1 O,OH
G2 H,O

Structure attributes must be viewed using STN Express query preparation.

=> s l1
SAMPLE SEARCH INITIATED 14:09:53 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 3614 TO ITERATE

55.3% PROCESSED 2000 ITERATIONS 50 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 68675 TO 75885
PROJECTED ANSWERS: 1268 TO 2418

L2 50 SEA SSS SAM L1

=> s l1 ful
FULL SEARCH INITIATED 14:09:58 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 72005 TO ITERATE

100.0% PROCESSED 72005 ITERATIONS 2128 ANSWERS
SEARCH TIME: 00.00.01

L3 2128 SEA SSS FUL L1

=> file zcaplus
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	172.10	172.31

FILE 'ZCAPLUS' ENTERED AT 14:10:14 ON 02 JUL 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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FILE COVERS 1907 - 2 Jul 2007 VOL 147 ISS 2
FILE LAST UPDATED: 1 Jul 2007 (20070701/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

```
=> s l3
L4          76 L3

=> d his

     (FILE 'HOME' ENTERED AT 14:09:22 ON 02 JUL 2007)

     FILE 'REGISTRY' ENTERED AT 14:09:33 ON 02 JUL 2007
L1              STRUCTURE UPLOADED
L2           50 S L1
L3         2128 S L1 FUL

     FILE 'ZCAPLUS' ENTERED AT 14:10:14 ON 02 JUL 2007
L4           76 S L3

=> d 14 1- ibib abs hitstr
YOU HAVE REQUESTED DATA FROM 76 ANSWERS - CONTINUE? Y/(N):y

L4   ANSWER 1 OF 76  ZCAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         2007:507562  ZCAPLUS
DOCUMENT NUMBER:          146:500897
TITLE:                    Preparation of pyrrolidinylpiperidines and related
                          compounds as antagonists of chemokine CCR2 inhibitors.
INVENTOR(S):              Ghosh, Shomir; Raman, Prakash; Sprott, Kevin; Elder,
                          Amy M.; Griffiths, Sian; Soucy, Francois; Ye, Qing
PATENT ASSIGNEE(S):       Millennium Pharmaceuticals, Inc., USA
SOURCE:                   PCT Int. Appl., 157pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE       APPLICATION NO.          DATE
     ---------------      ----   --------   --------------------     --------
     WO 2007053498         A1    20070510   WO 2006-US42180          20061026
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN,
             KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK,
             MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO,
             RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT,
             TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
         RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
             IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
             CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
             GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
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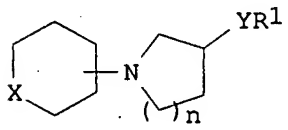
KG, KZ, MD, RU, TJ, TM
PRIORITY APPLN. INFO.: US 2005-732343P P 20051101
OTHER SOURCE(S): MARPAT 146:500897
GI



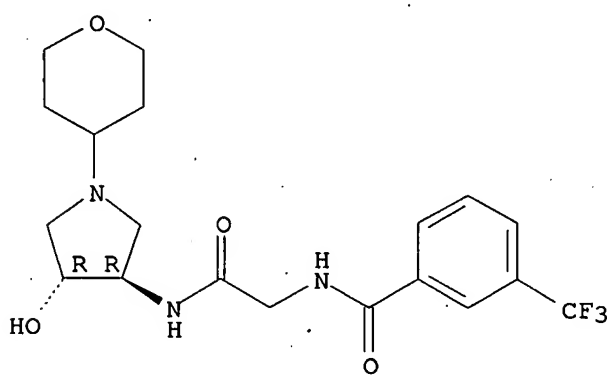
I

AB Title compds. [I; n = 1, 2; Y = Y1Y2, Y3Y4; Y1 = SO2NR', CONR', CONR'CO, NR'SO2NR'; Y2 = null, (substituted) (interrupted) alkylene, cycloalkylene, heterocyclylene, arylene, heteroarylene; Y3 = NR'CO, NR'CONR', NR'CO2; Y4 = (substituted) (interrupted) alkylene; R' = H, (substituted) aliphatyl; R1 = (substituted) cycloaliphatyl, heterocyclyl, heteroaryl; X = O, S, SO2, NWR4; W = null, W1L2W2; W1, W2 = null, (substituted) alkylene; L2 = null, NR, O, S, SO2, CO, CO2, CONR, etc.; R = H, alkyl; R4 = (substituted) cycloaliphatyl, heterocyclyl, heteroaryl], were prepared Thus, N-[2-oxo-2-[(3R)-pyrrolidin-3-ylamino]ethyl]-3-trifluoromethylbenzamide, 1-(6-methoxypyrrolidin-3-yl)piperidin-4-one (preparation given), and NaBH(OAc)3 were stirred together in MeOH to give N-[2-[[(3R)-1-[1-(6-methoxypyridin-3-yl)piperidin-4-yl]pyrrolidin-3-yl]amino]-2-oxoethyl]-3-trifluoromethylbenzamide. I have been shown to inhibit CCR2, preferably at <100 nM.

IT 936447-74-4P 936447-88-0P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of pyrrolidinylpiperidines and related compds. as antagonists of chemokine CCR2 inhibitors)

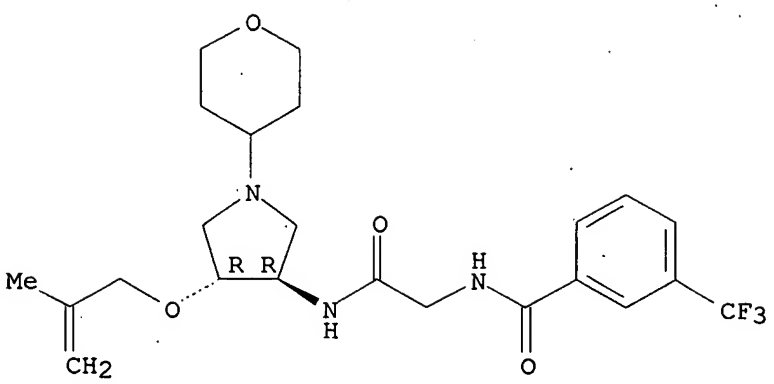
RN 936447-74-4 ZCAPLUS
CN Benzamide, N-[2-[[(3R,4R)-4-hydroxy-1-(tetrahydro-2H-pyran-4-yl)-3-pyrrolidinyl]amino]-2-oxoethyl]-3-(trifluoromethyl)-, rel- (CA INDEX NAME)

Relative stereochemistry.



RN 936447-88-0 ZCAPLUS
CN Benzamide, N-[2-[[(3R,4R)-4-[(2-methyl-2-propen-1-yl)oxy]-1-(tetrahydro-2H-pyran-4-yl)-3-pyrrolidinyl]amino]-2-oxoethyl]-3-(trifluoromethyl)-, rel- (CA INDEX NAME)

Relative stereochemistry.

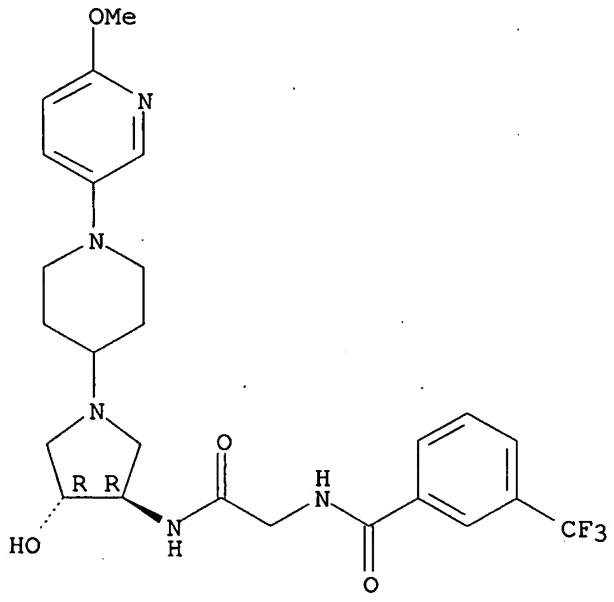


IT 936447-65-3P 936447-66-4P 936447-68-6P
936447-69-7P 936447-70-0P 936447-71-1P
936447-72-2P 936447-73-3P 936447-75-5P
936447-76-6P 936447-77-7P 936447-78-8P
936447-79-9P 936447-80-2P 936447-81-3P
936447-82-4P 936447-83-5P 936447-85-7P
936447-86-8P 936447-87-9P 936447-89-1P
936447-90-4P 936447-91-5P 936447-92-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyrrolidinylpiperidines and related compds. as antagonists of chemokine CCR2 inhibitors)

RN 936447-65-3 ZCAPLUS

CN Benzamide, N-[2-[[(3R,4R)-4-hydroxy-1-[1-(6-methoxy-3-pyridinyl)-4-piperidinyl]-3-pyrrolidinyl]amino]-2-oxoethyl]-3-(trifluoromethyl)-, rel- (CA INDEX NAME)

Relative stereochemistry.

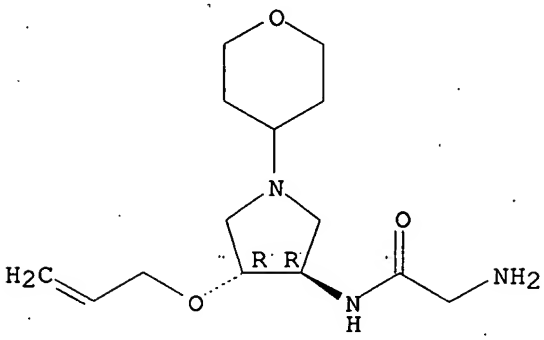


RN 936447-66-4 ZCAPLUS

CN Benzamide, N-[2-oxo-2-[[(3R,4R)-4-(2-pyridinylmethoxy)-1-(tetrahydro-2H-

RN 936448-07-6 ZCAPLUS
CN Acetamide, 2-amino-N-[(3R,4R)-4-(2-propen-1-yloxy)-1-(tetrahydro-2H-pyran-4-yl)-3-pyrrolidinyl]-, hydrochloride (1:2), rel- (CA INDEX NAME)

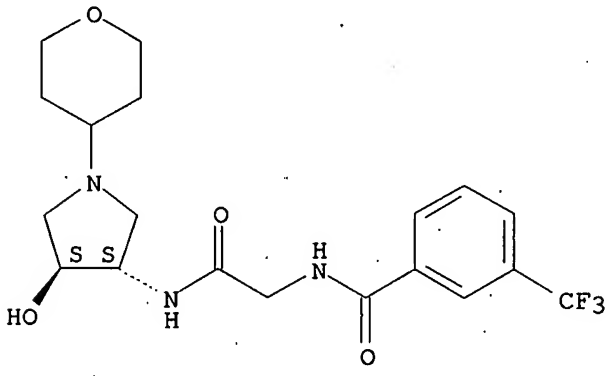
Relative stereochemistry.



●2 HCl

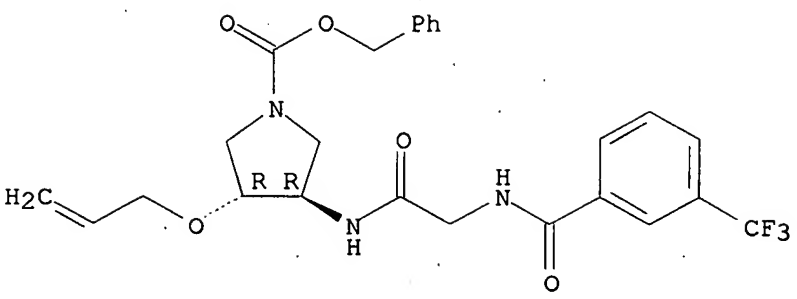
IT 936447-95-9P 936447-96-0P 936447-97-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of pyrrolidinylpiperidines and related compds. as antagonists of chemokine CCR2 inhibitors)
RN 936447-95-9 ZCAPLUS
CN Benzamide, N-[2-[[(3S,4S)-4-hydroxy-1-(tetrahydro-2H-pyran-4-yl)-3-pyrrolidinyl]amino]-2-oxoethyl]-3-(trifluoromethyl)- (CA INDEX NAME)

Absolute stereochemistry.



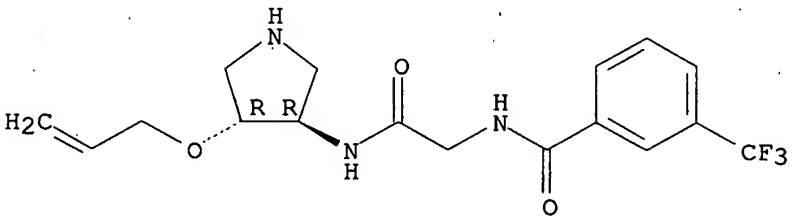
RN 936447-96-0 ZCAPLUS
CN INDEX NAME NOT YET ASSIGNED

Relative stereochemistry.



RN 936447-97-1 ZCAPLUS
CN Benzamide, N-[2-oxo-2-[[(3R,4R)-4-(2-propen-1-yloxy)-3-pyrrolidinyl]amino]ethyl]-3-(trifluoromethyl)-, rel- (CA INDEX NAME)

Relative stereochemistry.



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 76 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:113835 ZCAPLUS
DOCUMENT NUMBER: 146:190515
TITLE: Encapsulation of lipid-based formulations in enteric polymers
INVENTOR(S): McAllister, Stephen Mark
PATENT ASSIGNEE(S): Glaxo Group Limited, UK
SOURCE: PCT Int. Appl., 31pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007012478	A2	20070201	WO 2006-EP7387	20060724
WO 2007012478	A3	20070405		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,

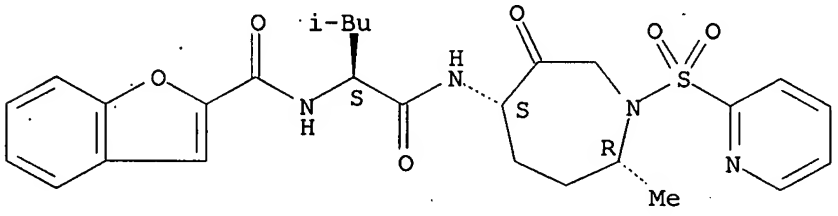
KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA
PRIORITY APPLN. INFO.: US 2005-702669P P 20050726

AB A microcapsule comprising a lipid-based core that is encapsulated in an enteric polymer shell providing enhanced bioavailability of a sparingly water-soluble drug as well as modulated release of the drug, wherein the microcapsule is, in one embodiment, prepared by a centrifugal coextrusion process is provided°. The lipid-based core comprises lipidic carriers, either liquid or solid (m.p. < 1000°), that would provide adequate drug solubilization and is compatible with the enteric shell materials. Thus, microcapsules containing a lipidic core comprising medium-chain triglycerides (Labrafac CC) 85%, polyglycolized glycerides (Gelucire 44/14) 10% and a sparingly water-soluble drug (SB 462795) 5%, and an enteric shell comprising HPMCP-55 22.4%, glycerin 1.4%, NaOH 3.2%, and water 73.0% were prepared with specific centrifugal coextrusion processing parameters and collection media of Dry-Flo or acetic acid diluted to 20% with water and trace amount of Tween 80. The resulting microcapsules showed negligible release in the dissoln. medium at acidic pH and rapid release and drug solubilization in a dissoln. medium that mimics intestinal fluid.

IT 362505-84-8, SB 462795
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(enteric polymers for encapsulation of lipid-based formulations comprising sparingly water-soluble drug)

RN 362505-84-8 ZCAPLUS
CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[(4S,7R)-hexahydro-7-methyl-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 3 OF 76 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1297449 ZCAPLUS
DOCUMENT NUMBER: 146:330734
TITLE: A highly potent inhibitor of cathepsin K (relacatib) reduces biomarkers of bone resorption both in vitro and in an acute model of elevated bone turnover in vivo in monkeys
AUTHOR(S): Kumar, S.; Dare, L.; Vasko-Moser, J. A.; James, I. E.; Blake, S. M.; Rickard, D. J.; Hwang, S.-M.; Tomaszek, T.; Yamashita, D. S.; Marquis, R. W.; Oh, H.; Jeong, J. U.; Veber, D. F.; Gowen, M.; Lark, M. W.; Stroup, G.
CORPORATE SOURCE: Department of Musculoskeletal Diseases, GlaxoSmithKline, Collegeville, PA, 19426, USA
SOURCE: Bone (San Diego, CA, United States) (2007), 40(1), 122-131
CODEN: BONEDL; ISSN: 8756-3282
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Cathepsin K is an osteoclast-derived cysteine protease that has been

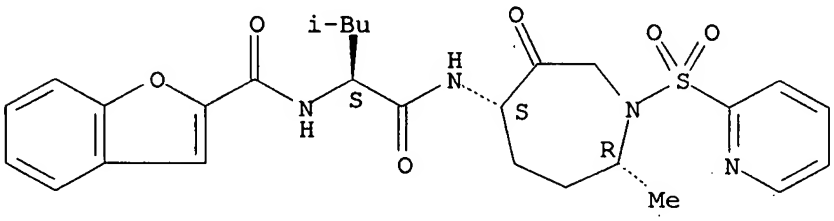
implicated as playing a major role in bone resorption. A substantial body of evidence indicates that cathepsin K is critical in osteoclast-mediated bone resorption and suggests that its pharmacol. inhibition should result in inhibition of bone resorption in vivo. Here we report the pharmacol. characterization of SB-462795 (relacatib) as a potent and orally bioavailable small mol. inhibitor of cathepsin K that inhibits bone resorption both in vitro in human tissue and in vivo in cynomolgus monkeys. SB-462795 is a potent inhibitor of human cathepsins K, L, and V (K i, app = 41, 68, and 53 pM, resp.) that exhibits 39-300-fold selectivity over other cathepsins. SB-462795 inhibited endogenous cathepsin K in situ in human osteoclasts and human osteoclast-mediated bone resorption with IC50 values of .apprx. 45 nM and .apprx. 70 nM, resp. The anti-resorptive potential of SB-462795 was evaluated in normal as well as medically ovariectomized (Ovx) female cynomolgus monkeys. Serum levels of the C- and N-terminal telopeptides of Type I collagen (CTx and NTx, resp.) and urinary levels of NTx were monitored as biomarkers of bone resorption. Administration of SB-462795 to medically ovariectomized or normal monkeys resulted in an acute reduction in both serum and urinary markers of bone resorption within 1.5 h after dosing, and this effect lasted up to 48 h depending on the dose administered. Our data indicate that SB-462795 potently inhibits human cathepsin K in osteoclasts, resulting in a rapid inhibition of bone resorption both in vitro and in vivo in the monkey. These studies also demonstrate the therapeutic potential of relacatib in the treatment of postmenopausal osteoporosis and serves to model the planned clin. trials in human subjects.

IT 362505-84-8, Relacatib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cathepsin K inhibitor relacatib reduced biomarkers of bone resorption in human osteoclast in vitro and in acute model of elevated bone turnover monkey model)

RN 362505-84-8 ZCAPLUS

CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[(4S,7R)-hexahydro-7-methyl-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 76 ZCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2006:1170547 ZCAPLUS

DOCUMENT NUMBER: 146:142984

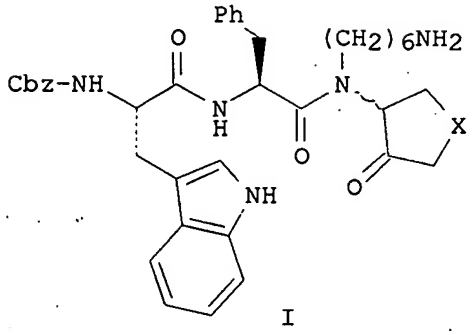
TITLE: Structure-activity studies of cyclic ketone inhibitors of the serine protease plasmin: design, synthesis, and biological activity

AUTHOR(S): Xue, Fengtian; Seto, Christopher T.

CORPORATE SOURCE: Department of Chemistry, Brown University, Providence, RI, 02912, USA

SOURCE: Bioorganic & Medicinal Chemistry (2006), 14(24), 8467-8487

CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 146:142984
GI



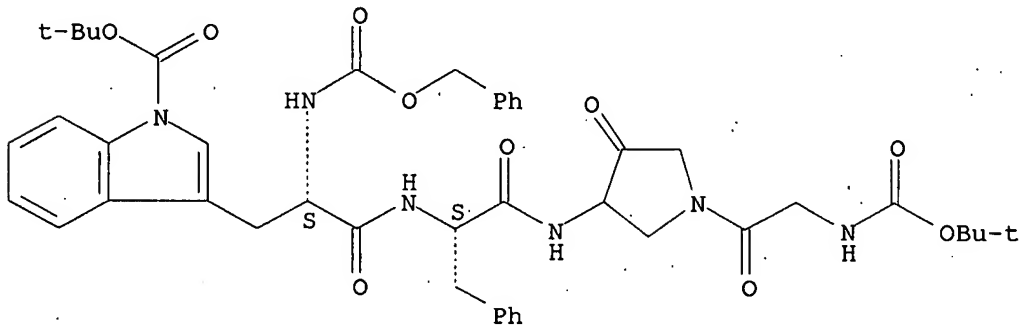
I

AB Three series of cyclic ketone inhibitors were synthesized and evaluated against the serine protease plasmin. Peptide inhibitors that incorporated 3-oxotetrahydrofuran and 3-oxotetrahydrothiophene 1,1-dioxide groups had the highest activities. Alkylamino substituents, which were designed to bind in the S1 subsite of plasmin, were attached to the inhibitors. Compds. I (X = O or SO2, Cbz = PhCH2O2C), which incorporated the 6-aminohexyl substituent, were found to be optimal and demonstrated IC50 values in the low micromolar range. Incorporating conformationally constrained peptide segments into the inhibitors did not improve their activities.

IT 918902-60-0P 918902-66-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and structure-activity of peptidyl cyclic ketone inhibitors of serine protease plasmin)

RN 918902-60-0 ZCAPLUS
CN Carbamic acid, N-[(1S)-2-[[(1S)-2-[[1-[2-[[(1,1-dimethylethoxy)carbonyl]amino]acetyl]-4-oxo-3-pyrrolidinyl]amino]-2-oxo-1-(phenylmethyl)ethyl]amino]-1-[[1-[(1,1-dimethylethoxy)carbonyl]-1H-indol-3-yl]methyl]-2-oxoethyl]-, phenylmethyl ester (CA INDEX NAME)

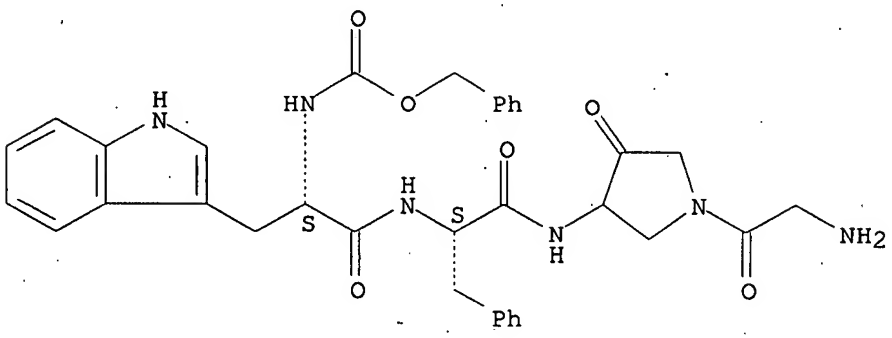
Absolute stereochemistry.



RN 918902-66-6 ZCAPLUS
CN Carbamic acid, N-[(1S)-2-[[(1S)-2-[[1-(2-aminoacetyl)-4-oxo-3-

pyrrolidinyl]amino]-2-oxo-1-(phenylmethyl)ethyl]amino]-1-(1H-indol-3-ylmethyl)-2-oxoethyl]-, phenylmethyl ester (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

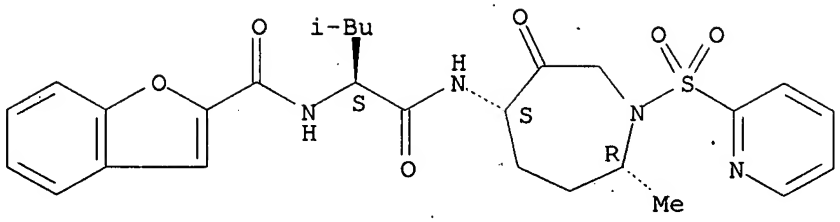
L4 ANSWER 5 OF 76 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:958469 ZCAPLUS
DOCUMENT NUMBER: 146:308057
TITLE: Relacatib: prevention and treatment of bone metastases, treatment of osteoarthritis, treatment on osteoporosis, cathepsin K inhibitor
AUTHOR(S): McIntyre, J. A.; Serradell, N.; Bolos, J.
CORPORATE SOURCE: Prous Science, Barcelona, 08080, Spain
SOURCE: Drugs of the Future (2006), 31(5), 406-411
CODEN: DRFUD4; ISSN: 0377-8282
PUBLISHER: Prous Science
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Cathepsin K is a cysteine protease synthesized by osteoclasts and one of the major effectors of osteoclastic bone resorption. As such, it is an attractive target for therapeutic intervention in the treatment of osteoporosis and other bone disorders causing bone degradation Relacatib (SB-462795) is a high-potency inhibitor of cathepsin K with demonstrated antiresorptive activity in normal and ovariectomized monkeys. Studies in ovariectomized monkeys also demonstrated a greater stimulatory effect on cortical bone compared to alendronate, with significant improvements in bone mineral d. and bone mineral content compared with vehicle-treated controls. Studies in monkeys indicate site-specific differences between alendronate and relacatib which may translate into differential efficacy. Relacatib is scheduled to enter phase II development for the prevention and treatment of bone metastases in 2006.

IT 362505-84-8P, Relacatib
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(SB-462795; relacatib was effective in prevention and treatment of bone metastases, osteoarthritis and osteoporosis in normal and ovariectomized monkey)

RN 362505-84-8 ZCAPLUS
CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[(4S,7R)-hexahydro-7-methyl-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

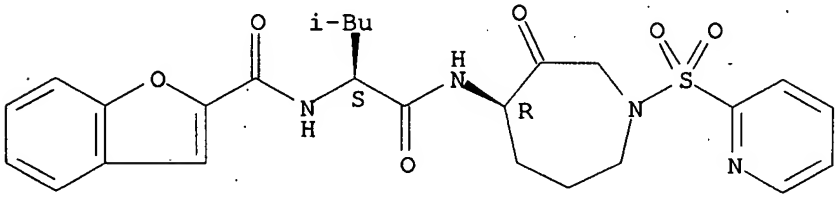
L4 ANSWER 6 OF 76 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:937462 ZCAPLUS
DOCUMENT NUMBER: 145:465162
TITLE: Substrate mapping and inhibitor profiling of falcipain-2, falcipain-3 and berghepain-2: Implications for peptidase anti-malarial drug discovery
AUTHOR(S): Ramjee, Manoj K.; Flinn, Nicholas S.; Pemberton, Tracy P.; Quibell, Martin; Wang, Yikang; Watts, John P.
CORPORATE SOURCE: Amura Therapeutics Limited, Horizon Park, Comberton, CB3 7AJ, UK
SOURCE: Biochemical Journal (2006), 399(1), 47-57
CODEN: BIJOAK; ISSN: 0264-6021
PUBLISHER: Portland Press Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The Plasmodium falciparum cysteine peptidases FP-2 (falcipain-2) and FP-3 (falcipain-3), members of the papain-like CAC1 family, are essential hemoglobinases and are therefore potential antimalarial drug targets. To facilitate a rational drug discovery program, in the current study the authors analyzed the synthetic substrate and model inhibitor profiles of FP-2 and FP-3 as well as BP-2 (berghepain-2), an ortholog from the rodent parasite Plasmodium berghei. With respect to substrate catalysis, FP-2 exhibited a promiscuous substrate profile based around a consensus nonprimeside motif, FP-3 was somewhat more restricted and BP-2 was comparatively specific. Substrate turnover for FP-2 was driven by a basic or acidic P1 residue, whereas for FP-3 turnover occurred predominately through a basic P1 residue only, and for BP-2, turnover was again mainly through a basic P1 residue for some motifs and surprisingly a glycine in the P1 position for other motifs. Within these P1 binding elements, addnl. recognition motifs were observed with subtle nuances that switched substrate turnover on or off through specific synergistic combinations. The peptidases were also profiled against reversible and irreversible cysteine peptidase inhibitors. The results reiterated the contrasting kinetic behavior of each peptidase as observed through the substrate screens. The results showed that the substrate and inhibitor preferences of BP-2 were markedly different from those of FP-2 and FP-3. When FP-2 and FP-3 were compared to each other they also displayed similarities and some significant differences. In conclusion, the in vitro data highlights the current difficulties faced by a peptidase directed antimalarial medicinal chemical program where compds. need to be identified with potent activity against at least three peptidases, each of which displays distinct biochem. traits.

IT 281214-75-3 281217-45-6
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(substrate mapping and inhibitor profiling of falcipain-2, falcipain-3 and berghepain-2 and implications for peptidase anti-malarial drug discovery)

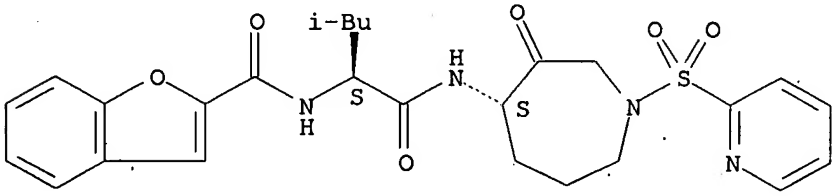
RN 281214-75-3 ZCAPLUS
CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[(4R)-hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 281217-45-6 ZCAPLUS
CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[(4S)-hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

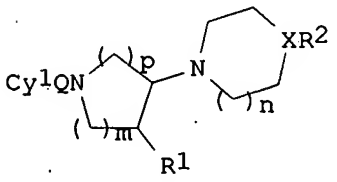
L4 ANSWER 7 OF 76 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:654015 ZCAPLUS
DOCUMENT NUMBER: 145:124609
TITLE: Preparation of piperidinyl- and (homo)piperazinylpyrrolidinols as chemokine receptor antagonists.
INVENTOR(S): Rosse, Gerard; Wei, Linli; Carson, Kenneth G.
PATENT ASSIGNEE(S): Millennium Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 172 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006071958	A1	20060706	WO 2005-US47327	20051228

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,

IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

US 2006189628 A1 20060824 US 2005-320298 20051228
PRIORITY APPLN. INFO.: US 2004-639913P P 20041229
OTHER SOURCE(S): MARPAT 145:124609
GI



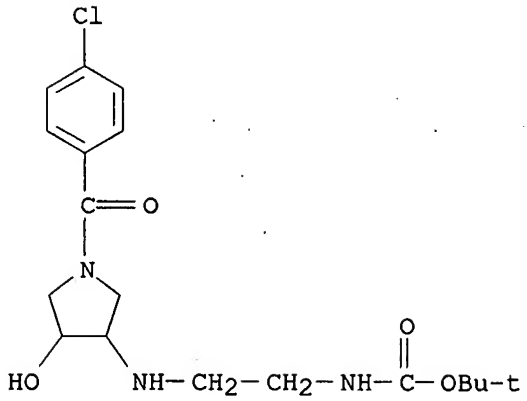
I

AB Title compds. [I; m, n, p = 1, 2; R1 = F, R3, OR4, SR4, CO2R4, COR4, CON(R4)2, N(R4)2, SO2N(R4)2, OSO2R4, CON(R4)2, etc.; R3 = (substituted) aliphatyl, (aromatic) (heterocyclic) monocyclic ring; R4 = H, R3; N(R4)2 = (substituted) 3-6 membered (aromatic) (heterocyclic) ring; R2 = T-Cy2, Cy2; T = null, (substituted) (heteroatom-interrupted) alkylene; Cy2 = (substituted) 3-7 membered (aromatic) (heterocyclic) (bicyclic) ring; Cy1 = (substituted) 5-8 membered (aromatic) (heterocyclic) ring, 8-14 membered bi- or tricyclic (heterocyclic) ring; X = N, CR8; R8 = F, cyano, R9, OR9, SR9, CO2R9, N(R9)2, SO2N(R9)2, COR9, etc.; R9 = H, (substituted) aliphatyl; Q = (substituted) (heteroatom-interrupted) alkylene; rings may be addnl. substituted], were prepared Thus, (3RS,4RS)-4-(4-chlorophenyl)-1-(4-hydroxypyrrolidin-3-yl)piperidin-4-ol bistrifluoroacetate (preparation given), diisopropylethylamine, diphenylacetic acid, and HATU were stirred together in DMF to give (3RS,4RS)-1-[3-[4-(4-chlorophenyl)-4-hydroxypiperidin-1-yl]-4-hydroxypyrrolidin-1-yl]-2,2-diphenylethanone trifluoroacetate. Many I inhibited CCR1 with activity at <1 μM.

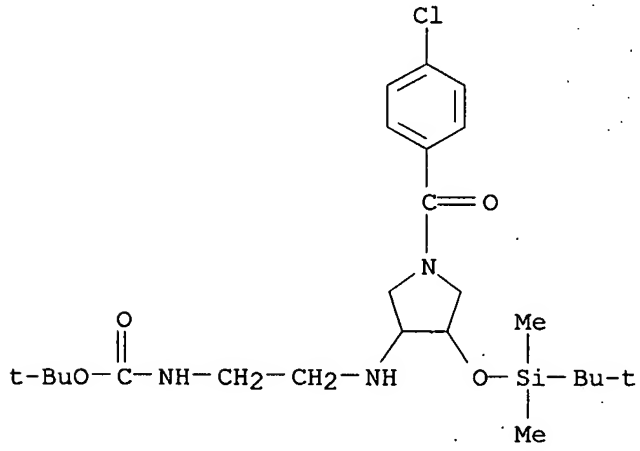
IT 897652-10-7P 897652-11-8P 897652-12-9P
897652-13-0P 897652-24-3P 897652-25-4P
897652-26-5P 897652-27-6P 897652-28-7P
897654-30-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of piperidinyl- and (homo)piperazinylpyrrolidinols as chemokine receptor antagonists)

RN 897652-10-7 ZCAPLUS

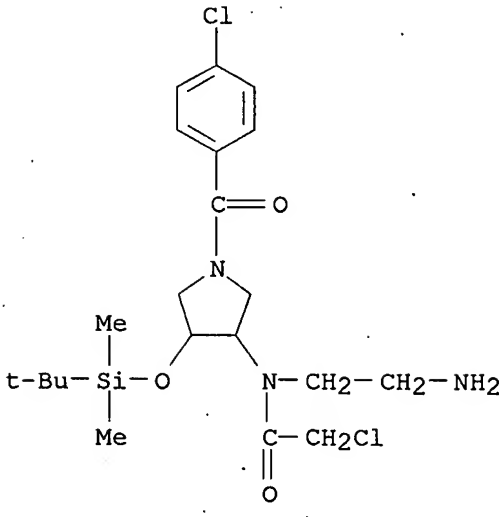
CN Carbamic acid, [2-[[1-(4-chlorobenzoyl)-4-hydroxy-3-pyrrolidinyl]amino]ethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 897652-11-8 ZCAPLUS
CN Carbamic acid, [2-[[1-(4-chlorobenzoyl)-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3-pyrrolidinyl]amino]ethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 897652-12-9 ZCAPLUS
CN Carbamic acid, [2-[(chloroacetyl)[1-(4-chlorobenzoyl)-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3-pyrrolidinyl]amino]ethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 8 OF 76 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:367270 ZCAPLUS
DOCUMENT NUMBER: 144:398367
TITLE: Amorphous pharmaceutical compositions comprising rosiglitazone
INVENTOR(S): Ignatious, Francis; Sun, Linghong; Craig, Andrew; Crowe, David; Ho, Tim; Millan, Michael
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: U.S. Pat. Appl. Publ., 36 pp., Cont.-in-part of U.S. Ser. No. 523,835.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006083784	A1	20060420	US 2005-64890	20050224
WO 2004014304	A2	20040219	WO 2003-US24641	20030807
WO 2004014304	A3	20040624		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2006013869	A1	20060119	US 2005-523835	20050207
WO 2006090150	A1	20060831	WO 2006-GB632	20060223
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX,				

MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.:

US 2002-401726P	P	20020807
WO 2003-US24641	W	20030807
US 2005-523835	A2	20050207
US 2005-64890	A	20050224

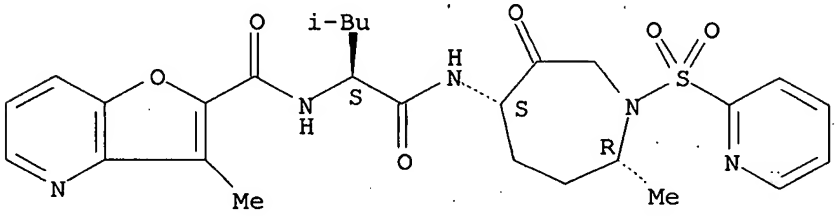
AB The present invention is directed to use of electrospinning, i.e. the process of making polymer nanofibers from either a solution or melt under elec. forces, to prepare stable, solid dispersions of amorphous drugs in polymer nanofibers. The present invention is also directed to the process of making solid dispersions of amorphous forms and compns. of rosiglitazone and its pharmaceutically acceptable salts. A 3.1 weight% solution of rosiglitazone mesylate 2-PrOH-water was spray dried to give an amorphous powder.

IT 362505-94-0
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amorphous pharmaceutical compns. comprising rosiglitazone)

RN 362505-94-0 ZCAPLUS

CN Furo[3,2-b]pyridine-2-carboxamide, N-[(1S)-1-[[[(4S,7R)-hexahydro-7-methyl-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]-3-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



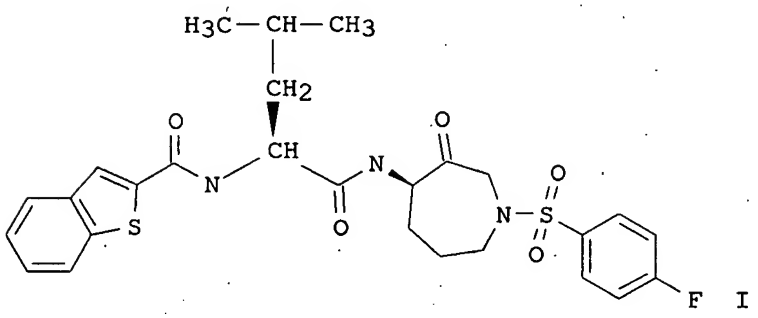
L4 ANSWER 9 OF 76 ZCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2006:238476 ZCAPLUS
DOCUMENT NUMBER: 144:286221
TITLE: Method for activating TRPV4 channel receptors by agonists and reducing the breakdown of an extracellular matrix
INVENTOR(S): Kumar, Sanjay; Pratta, Michael A.; Votta, Bartholomew Jude
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 76 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2006029209 A2 20060316 WO 2005-US31872 20050907
WO 2006029209 A3 20070329
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
EP 1796677 A2 20070620 EP 2005-795258 20050907
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU
PRIORITY APPLN. INFO.: US 2004-607544P P 20040907
WO 2005-US31872 W 20050907

GI



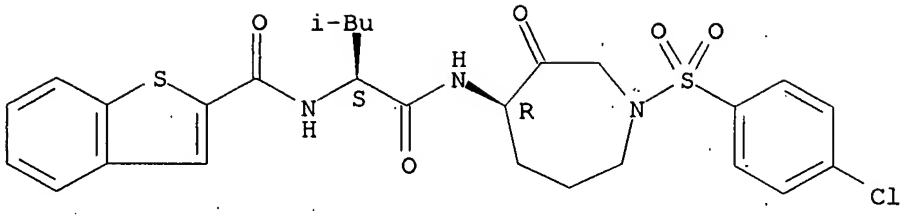
AB The invention discloses methods for activating a TRPV4 channel receptor, thereby reducing the production and/or release of matrix degrading enzymes by a cell expressing a TRPV4 channel receptor, thereby reducing the breakdown of an extracellular matrix. Also contemplated are methods for attenuating the inhibition of matrix production Preparation and activity of azepine compds., e.g. I, is included.

IT 281216-32-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(activation of TRPV4 channel receptors by agonists and reduction of breakdown of extracellular matrix)

RN 281216-32-8 ZCAPLUS

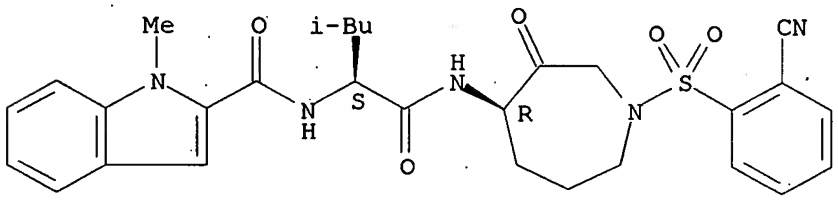
CN Benzo[b]thiophene-2-carboxamide, N-[(1S)-1-[[[(4R)-1-[(4-chlorophenyl)sulfonyl]hexahydro-3-oxo-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



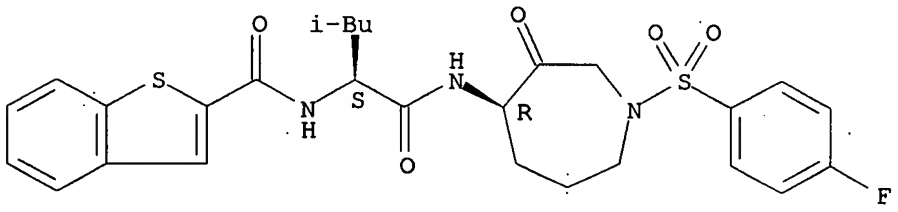
IT 281215-87-0 281216-61-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(activation of TRPV4 channel receptors by agonists and reduction of breakdown of extracellular matrix)
RN 281215-87-0 ZCAPLUS
CN 1H-Indole-2-carboxamide, N-[(1S)-1-[[[(4R)-1-[(2-cyanophenyl)sulfonyl]hexahydro-3-oxo-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]-1-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



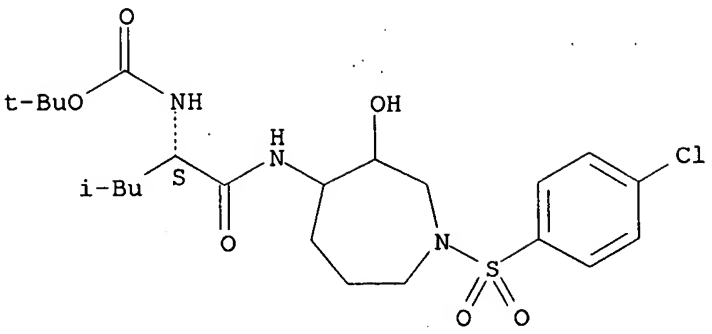
RN 281216-61-3 ZCAPLUS
CN Benzo[b]thiophene-2-carboxamide, N-[(1S)-1-[[[(4R)-1-[(4-fluorophenyl)sulfonyl]hexahydro-3-oxo-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



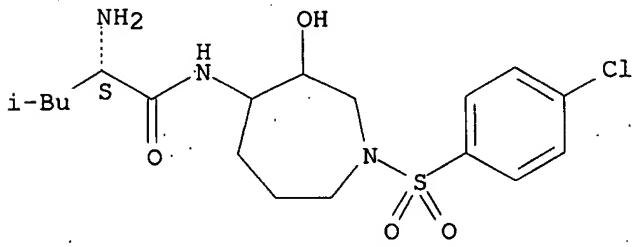
IT 281221-14-5P 281221-15-6P 878649-33-3P
878649-34-4P 878649-35-5P 878649-36-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(activation of TRPV4 channel receptors by agonists and reduction of breakdown of extracellular matrix)
RN 281221-14-5 ZCAPLUS
CN Carbamic acid, [(1S)-1-[[[1-[(4-chlorophenyl)sulfonyl]hexahydro-3-hydroxy-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



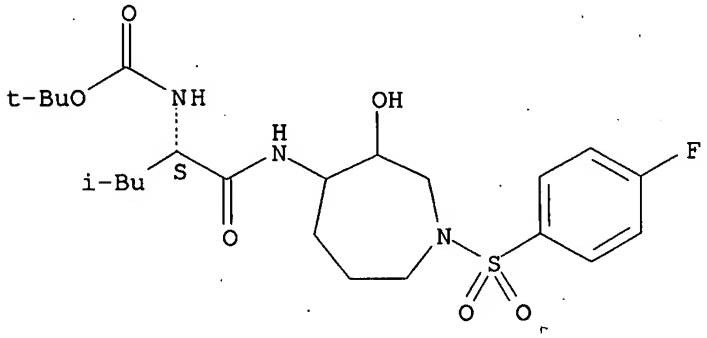
RN 281221-15-6 ZCAPLUS
CN Pentanamide, 2-amino-N-[1-[(4-chlorophenyl)sulfonyl]hexahydro-3-hydroxy-1H-azepin-4-yl]-4-methyl-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



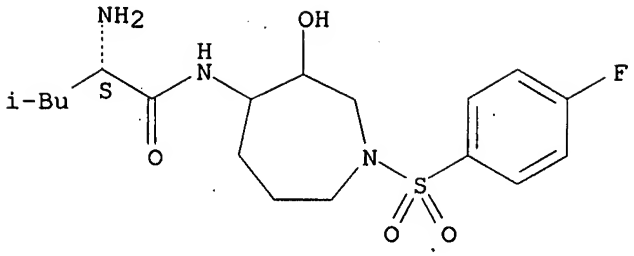
RN 878649-33-3 ZCAPLUS
CN Carbamic acid, [(1S)-1-[[[1-[(4-fluorophenyl)sulfonyl]hexahydro-3-hydroxy-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 878649-34-4 ZCAPLUS
CN Pentanamide, 2-amino-N-[1-[(4-fluorophenyl)sulfonyl]hexahydro-3-hydroxy-1H-azepin-4-yl]-4-methyl-, monohydrochloride, (2S)- (9CI) (CA INDEX NAME)

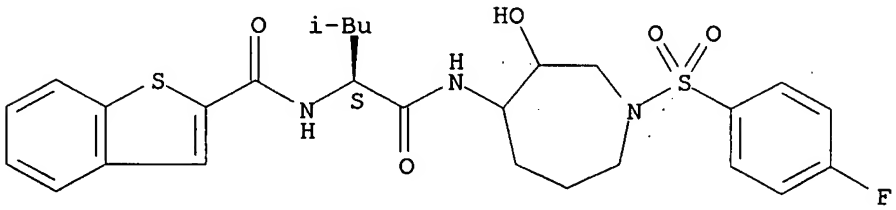
Absolute stereochemistry.



● HCl

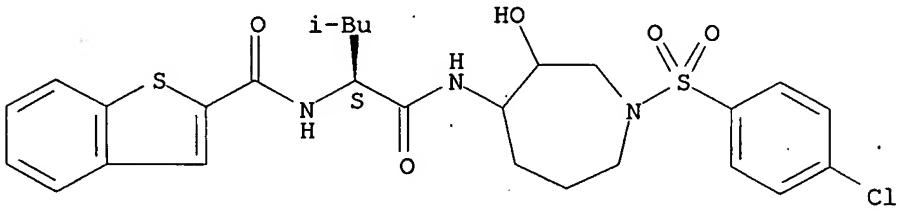
RN 878649-35-5 ZCAPLUS
CN Benzo[b]thiophene-2-carboxamide, N-[(1S)-1-[[[1-[(4-fluorophenyl)sulfonyl]hexahydro-3-hydroxy-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 878649-36-6 ZCAPLUS
CN Benzo[b]thiophene-2-carboxamide, N-[(1S)-1-[[[1-[(4-chlorophenyl)sulfonyl]hexahydro-3-hydroxy-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 10 OF 76 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:153597 ZCAPLUS
DOCUMENT NUMBER: 144:369900
TITLE: Synthesis of 3-oxoazacyclohept-4-enes by ring-closing metathesis. Application to the synthesis of an inhibitor of cathepsin K
AUTHOR(S): Taillier, Catherine; Hameury, Thomas; Bellosta, Veronique; Cossy, Janine
CORPORATE SOURCE: Laboratoire de Chimie Organique, associe au CNRS, ESPCI, Paris, 75231/05, Fr.
SOURCE: Heterocycles (2006), 67(2), 549-554
CODEN: HTCYAM; ISSN: 0385-5414

PUBLISHER: Japan Institute of Heterocyclic Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 144:369900

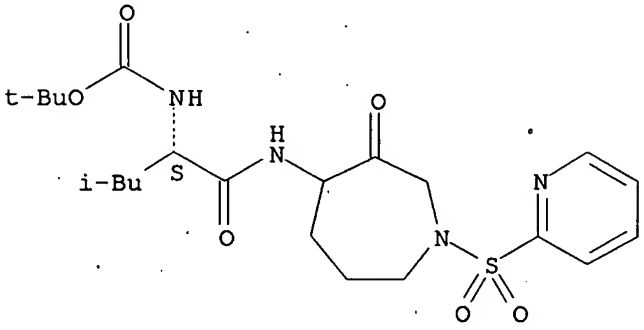
AB The ring-closing metathesis allows the formation of 3-oxoazacyclohept-4-enes from but-3-enamine. By using this methodol., the synthesis of an inhibitor of cathepsin K was achieved in 10 steps from but-3-enamine.

IT 882529-78-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of azacycloheptenones by ring-closing metathesis)

RN 882529-78-4 ZCAPLUS

CN Carbamic acid, [(1S)-1-[[[hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

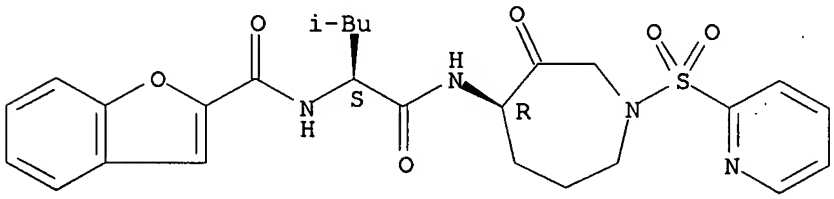


IT 281214-75-3P 281217-45-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of azacycloheptenones by ring-closing metathesis)

RN 281214-75-3 ZCAPLUS

CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[(4R)-hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

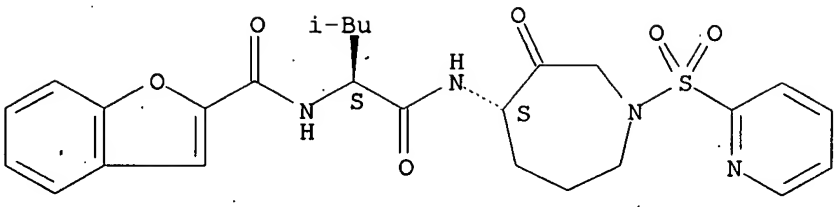
Absolute stereochemistry.



RN 281217-45-6 ZCAPLUS

CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[(4S)-hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 11 OF 76 ZCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2006:137811 ZCAPLUS
DOCUMENT NUMBER: 144:390724

TITLE: Structure Activity Relationships of 5-, 6-, and 7-Methyl-Substituted Azepan-3-one Cathepsin K Inhibitors

AUTHOR(S): Yamashita, Dennis S.; Marquis, Robert W.; Xie, Ren; Nidamarthy, Sirishkumar D.; Oh, Hye-Ja; Jeong, Jae U.; Erhard, Karl F.; Ward, Keith W.; Roethke, Theresa J.; Smith, Brian R.; Cheng, H-Y.; Geng, Xiaoliu; Lin, Fan; Offen, Priscilla H.; Wang, Bing; Nevins, Neysa; Head, Martha S.; Haltiwanger, R. Curtis; Narducci Sarjeant, Amy A.; Liable-Sands, Louise M.; Zhao, Baoguang; Smith, Ward W.; Janson, Cheryl A.; Gao, Enoch; Tomaszek, Thaddeus; McQueney, Michael; James, Ian E.; Gress, Catherine J.; Zembryki, Denise L.; Lark, Michael W.; Veber, Daniel F.

CORPORATE SOURCE: Department of Medicinal Chemistry, GlaxoSmithKline, Collegeville, PA, 19426, USA

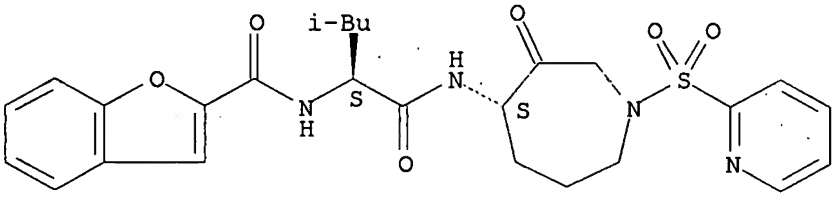
SOURCE: Journal of Medicinal Chemistry (2006), 49(5), 1597-1612
CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The syntheses, in vitro characterizations, and rat and monkey in vivo pharmacokinetic profiles of a series of 5-, 6-, and 7-methyl-substituted azepanone-based cathepsin K inhibitors are described. Depending on the particular regiochem. substitution and stereochem. configuration, methyl-substituted azepanones were identified that had widely varied cathepsin K inhibitory potency as well as pharmacokinetic properties compared to the 4S-parent azepanone analog, benzofuran-2-carboxylic acid [(1S)-3-methyl-1-[[(4S)-3-oxo-1-(pyridine-2-sulfonyl)azepan-4-yl]carbamoyl]butyl]amide (human cathepsin K, Ki,app = 0.16 nM, rat oral bioavailability = 42%, rat in vivo clearance = 49.2 mL/min/kg). Of particular note, one 4S-7-cis-methylazepanone analog (I; Relacatib) had a Ki,app = 0.041 nM vs human cathepsin K and 89% oral bioavailability and an in vivo clearance rate of 19.5 mL/min/kg in the rat. Hypotheses that rationalize some of the observed characteristics of these closely related analogs have been made using X-ray crystallog. and conformational anal. These examples demonstrate the potential for modulation of pharmacol. properties of cathepsin inhibitors by substituting the azepanone core. The high potency for inhibition of cathepsin K coupled with the favorable rat and monkey pharmacokinetic characteristics of I, also known as SB-462795 or Relacatib, has made it the subject of considerable in vivo evaluation for safety and efficacy as an inhibitor of excessive bone resorption in rat, monkey, and human studies, which will be reported elsewhere.

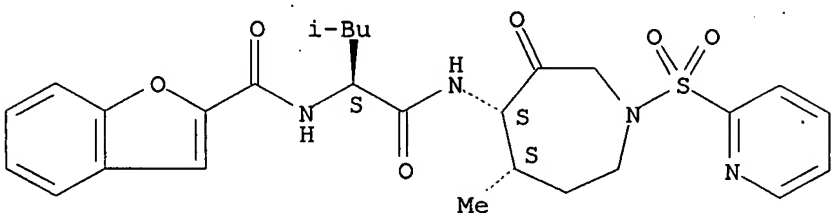
IT 281217-45-6, Benzofuran-2-carboxylic acid [(1S)-3-methyl-1-[[(4S)-3-oxo-1-(pyridine-2-sulfonyl)azepan-4-yl]carbamoyl]butyl]amide
RL: PAC (Pharmacological activity); BIOL (Biological study)
(preparation of chiral N-[[hexahydro(oxo)(pyridinylsulfonyl)azepinyl]amino]carbonyl]methylbutyl]benzofurancarboxamide derivs. and study of their activity as human cathepsin K inhibitors)
RN 281217-45-6 ZCAPLUS
CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[(4S)-hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



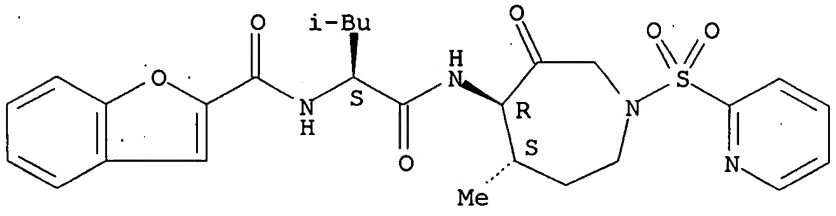
IT 362507-34-4P 362507-43-5P 883198-33-2P
883198-34-3P 883198-35-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of chiral N-[[hexahydro(oxo)(pyridinylsulfonyl)azepinyl]amino]carbonyl]methylbutyl]benzofurancarboxamide derivs. and study of their activity as human cathepsin K inhibitors)
RN 362507-34-4 ZCAPLUS
CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[(4S,5S)-hexahydro-5-methyl-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



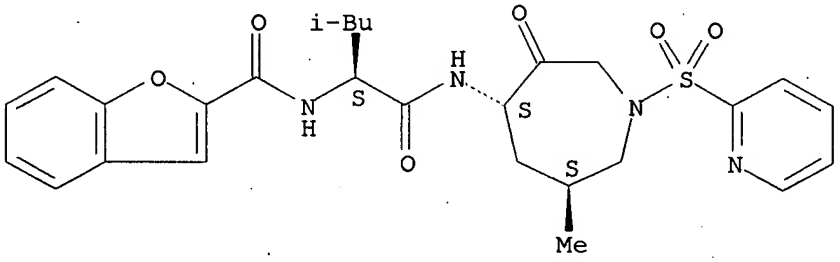
RN 362507-43-5 ZCAPLUS
CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[(4R,5S)-hexahydro-5-methyl-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



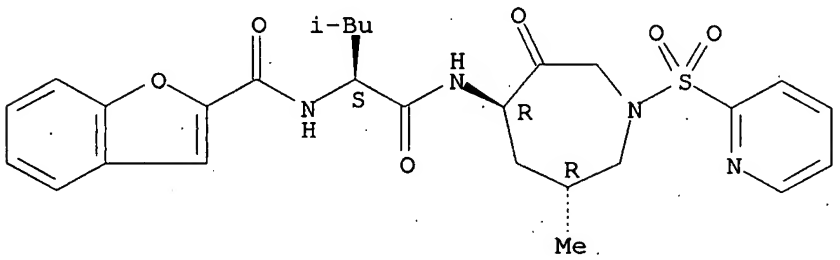
RN 883198-33-2 ZCAPLUS
CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[(4S,6S)-hexahydro-6-methyl-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



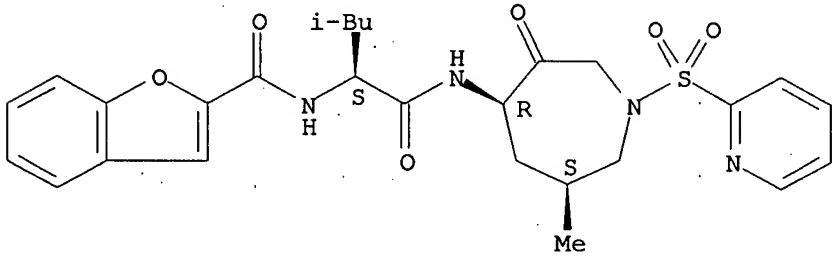
RN 883198-34-3 ZCAPLUS
CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[(4R,6R)-hexahydro-6-methyl-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

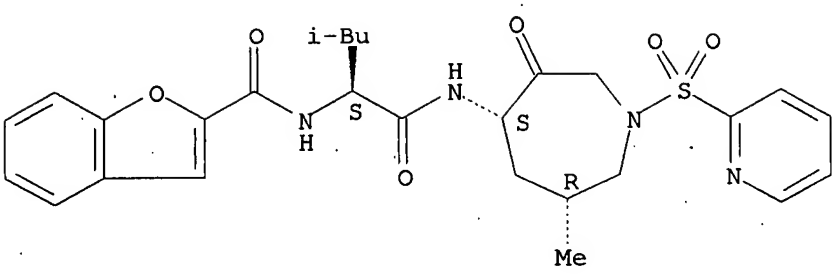


RN 883198-35-4 ZCAPLUS
CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[(4R,6S)-hexahydro-6-methyl-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 362632-37-9P 362632-39-1P 362632-40-4P
362632-41-5P 362632-43-7P 403700-44-7P
403700-45-8P 403700-48-1P 883198-47-8P
883231-92-3P 883231-93-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of chiral N-[[hexahydro(oxo)(pyridinylsulfonyl)azepinyl]amino]c

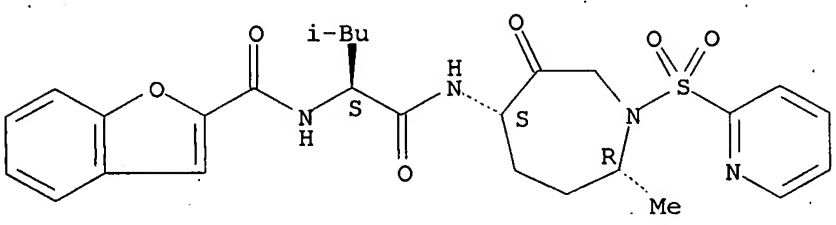


IT 362505-84-8DP, Relacatib, complex with human cathepsin K
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(preparation of chiral N-[[hexahydro(oxo)(pyridinylsulfonyl)azepinyl]amino]carbonyl]methylbutyl]benzofurancarboxamide, study of its activity as human cathepsin K inhibitor and study of its crystal and mol. structures)

RN 362505-84-8 ZCAPLUS

CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[(4S,7R)-hexahydro-7-methyl-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 12 OF 76 ZCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:1059040 ZCAPLUS

DOCUMENT NUMBER: 143:460415

TITLE: Azepanone-Based Inhibitors of Human Cathepsin L

AUTHOR(S): Marquis, Robert W.; James, Ian; Zeng, Jin; Trout, Robert E. Lee; Thompson, Scott; Rahman, Attiq; Yamashita, Dennis S.; Xie, Ren; Ru, Yu; Gress, Catherine J.; Blake, Simon; Lark, Michael A.; Hwang, Shing-Mei; Tomaszek, Thaddeus; Offen, Priscilla; Head, Martha S.; Cummings, Maxwell D.; Veber, Daniel F.

CORPORATE SOURCE: Departments of Medicinal Chemistry, Bone and Cartilage Biology Molecular Recognition and Physical and Structural Chemistry, GlaxoSmithKline, Collegeville, PA, 19426, USA

SOURCE: Journal of Medicinal Chemistry (2005), 48(22), 6870-6878
CODEN: JMCMAR; ISSN: 0022-2623

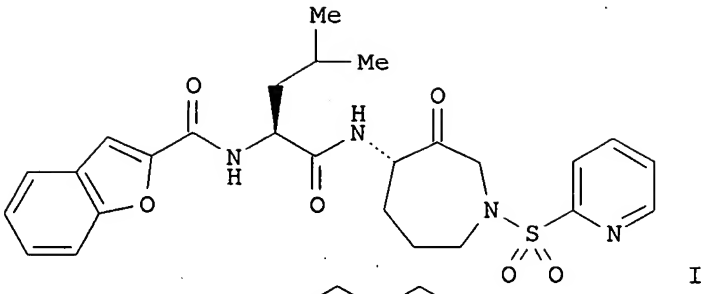
PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

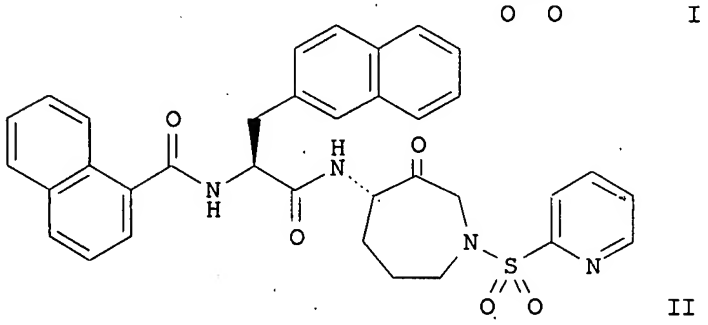
LANGUAGE: English

OTHER SOURCE(S): CASREACT 143:460415

GI



I



II

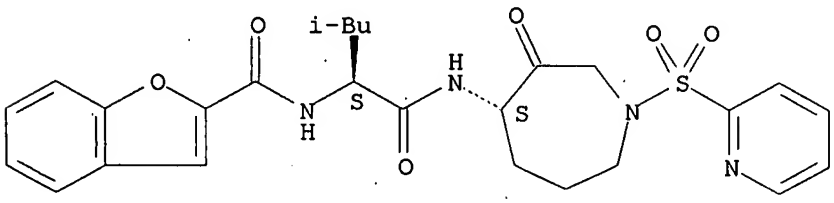
AB The extension of a previously-reported cathepsin K azepanone-based inhibitor template to the design and synthesis of potent and selective inhibitors of the homologous cysteine protease cathepsin L is detailed. Structure-activity studies examining the effect of inhibitor selectivity as a function of the P3 and P2 binding elements of the potent cathepsin K inhibitor leucinamide derivative I revealed that incorporation of either a P3 quinoline-8-carboxamide or a naphthalene-1-carboxamide led to increased selectivity for cathepsin L over cathepsin K. Substitution of the P2 leucine of I with either a phenylalanine or a β-naphthylalanine also resulted in an increased selectivity for cathepsin L over cathepsin K. Mol. modeling studies with the inhibitors docked within the active sites of both cathepsins L and K have rationalized the observed selectivities. Optimization of cathepsin L binding by the combination of the P3 naphthalene-1-carboxamide with the P2 β-naphthylalanine provided β-naphthylalaninamide derivative II, which is a potent, selective, and competitive inhibitor of human cathepsin L with a Ki = 0.43 nM.

IT 281217-45-6
RL: PAC (Pharmacological activity); BIOL (Biological study)
(preparation and structure-activity studies of azepanone-derived inhibitors of cathepsin)

RN 281217-45-6 ZCAPLUS

CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[(4S)-hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



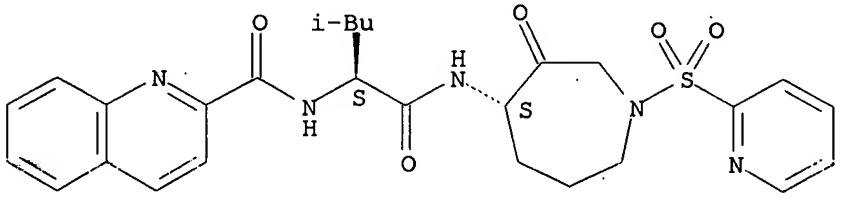
IT 281217-48-9P 869302-02-3P
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic

preparation); BIOL (Biological study); PREP (Preparation)
(preparation and structure-activity studies of azepanone-derived inhibitors of cathepsin)

RN 281217-48-9 ZCAPLUS

CN 2-Quinolinecarboxamide, N-[(1S)-1-[[[(4S)-hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

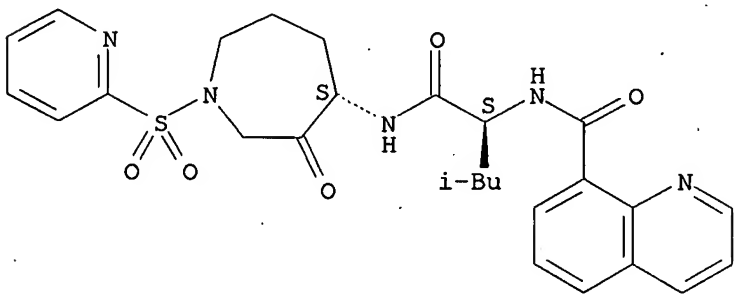
Absolute stereochemistry.



RN 869302-02-3 ZCAPLUS

CN 8-Quinolinecarboxamide, N-[(1S)-1-[[[(4S)-hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

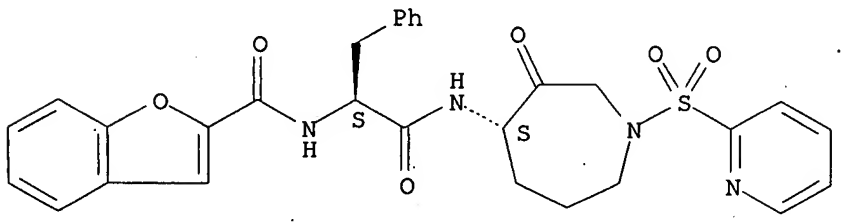


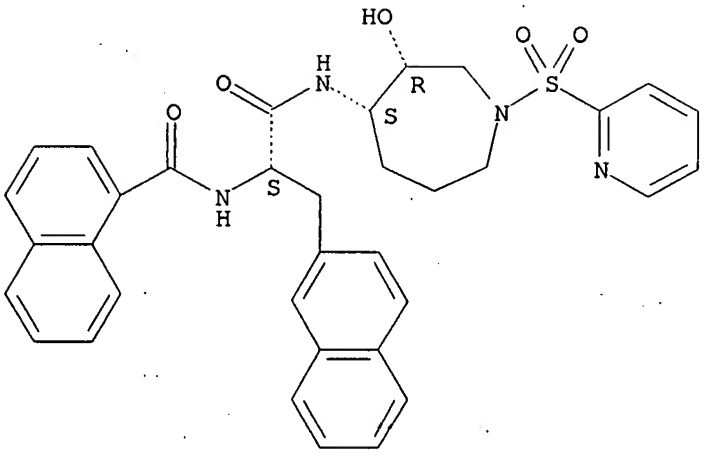
IT 281218-61-9P 281219-03-2P 350796-39-3P
869302-03-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and structure-activity studies of azepanone-derived inhibitors of cathepsin)

RN 281218-61-9 ZCAPLUS

CN 2-Benzofurancarboxamide, N-[(1S)-2-[[(4S)-hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]-2-oxo-1-(phenylmethyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.





REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 13 OF 76 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:696725 ZCAPLUS
DOCUMENT NUMBER: 143:179625
TITLE: Encapsulation of lipid-based formulations in enteric polymers
INVENTOR(S): Pillai, Raviraj S.
PATENT ASSIGNEE(S): Glaxo Group Limited, UK
SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005070401	A1	20050804	WO 2005-US1134	20050113
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1708687	A1	20061011	EP 2005-711432	20050113
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, HR, IS				

PRIORITY APPLN. INFO.: US 2004-537131P P 20040116
WO 2005-US1134 W 20050113

AB A microcapsule comprising a lipid-based core that is encapsulated in an enteric polymer shell providing enhanced bioavailability of a sparingly water-soluble drug as well as modulated release of the drug, wherein the microcapsule is, in one embodiment, prepared by a centrifugal coextrusion process. The lipid-based core comprises lipids carriers, either liquid or solid (m.p. < 100°C), that would provide adequate drug

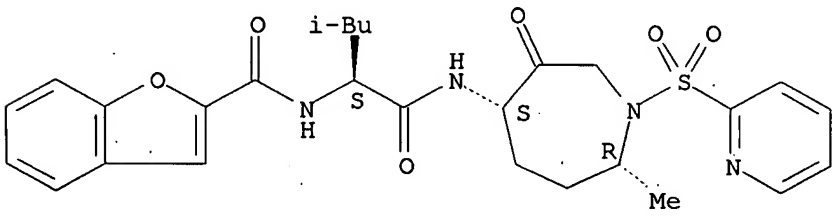
solubilization and is compatible with the enteric shell materials. For example, microcapsules containing a lipidic core comprising a medium chain triglyceride and a sparingly water-soluble drug (SB 462795) and an enteric shell comprising HPMCP-55 were prepared A core contained Labrafac CC 85%, polyglycolized glycerides (Gelucire 44/14) 10%, and SB 462795 5%, and shell contained water 73.0%, NaOH 3.2%, HPMCP-55 22.4%, and glycerin 1.4%. The resulting microcapsule had poor aqueous solubility (< 5 pg/mL). The microcapsules showed negligible drug release in the dissoln. medium at acidic pH and rapid release and drug solubilization in a dissoln. medium that mimics intestinal fluid. The microcapsules can be filled directly into capsule shells or blended with granules containing a different active and then filled into capsule shells suitable for dosing.

IT 362505-84-8, SB 462795
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(encapsulation of lipid-based formulations of sparingly water-soluble drug in enteric polymers)

RN 362505-84-8 ZCAPLUS

CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[(4S,7R)-hexahydro-7-methyl-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 14 OF 76 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:696636 ZCAPLUS
DOCUMENT NUMBER: 143:193920
TITLE: A preparation of derivatives of benzofuran-2-carboxylic acid amide, useful as cysteine protease inhibitors
INVENTOR(S): Clark, William M.; Badham, Neil Francis; Dai, Qunying; Eldridge, Ann Marie; Matsuhashi, Hayao
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005069981	A2	20050804	WO 2005-US2121	20050121
WO 2005069981	A3	20060126		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, SM

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1713790 A2 20061025 EP 2005-722504 20050121

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, HR, IS

PRIORITY APPLN. INFO.: US 2004-538861P P 20040123

WO 2005-US2121 W 20050121

OTHER SOURCE(S): CASREACT 143:193920

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to a preparation of derivs. of benzofuran-2-carboxylic acid amide, useful as cysteine protease inhibitors (no biol. data). For instance, benzofuran derivative I was prepared via amidation of carboxylic acid II by amine III and subsequent oxidation (yield of amidation was 90%).

IT 362507-77-5P 362507-85-5P

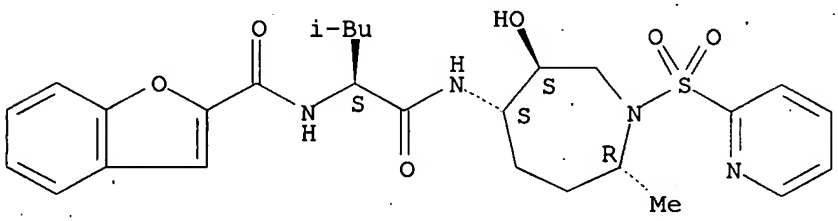
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of derivs. of benzofuran-2-carboxylic acid amide useful as cysteine protease inhibitors)

RN 362507-77-5 ZCAPLUS

CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[(3S,4S,7R)-hexahydro-3-hydroxy-7-methyl-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

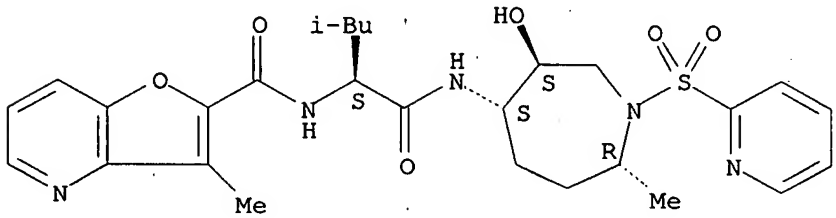
Absolute stereochemistry.



RN 362507-85-5 ZCAPLUS

CN Furo[3,2-b]pyridine-2-carboxamide, N-[(1S)-1-[[[(3S,4S,7R)-hexahydro-3-hydroxy-7-methyl-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]-3-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



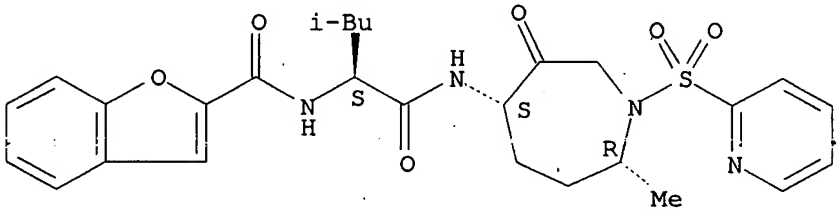
IT 362505-84-8P 362505-94-0P

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of derivs. of benzofuran-2-carboxylic acid amide useful as cysteine protease inhibitors)

RN 362505-84-8 ZCAPLUS

CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[(4S,7R)-hexahydro-7-methyl-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (CA INDEX NAME)

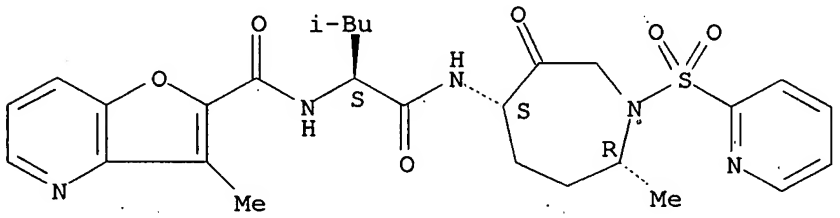
Absolute stereochemistry.



RN 362505-94-0 ZCAPLUS

CN Furo[3,2-b]pyridine-2-carboxamide, N-[(1S)-1-[[[(4S,7R)-hexahydro-7-methyl-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]-3-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 15 OF 76 ZCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:638869 ZCAPLUS

DOCUMENT NUMBER: 143:133700

TITLE: Preparation of peptides as cathepsin cysteine protease inhibitors

INVENTOR(S): Bayly, Christopher; Black, Cameron; Therien, Michel

PATENT ASSIGNEE(S): Merck Frosst Canada & Co., Can.

SOURCE: PCT Int. Appl., 62 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005066159	A1	20050721	WO 2005-CA7	20050106

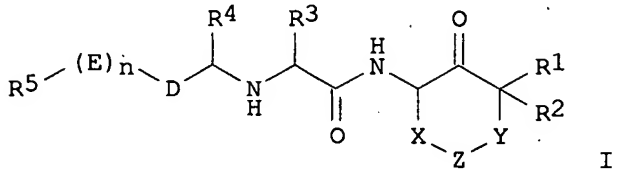
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

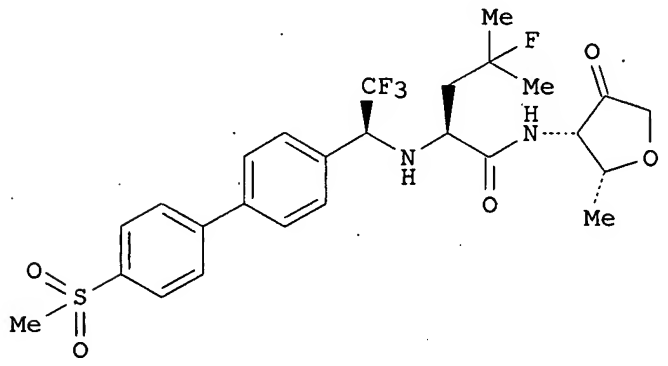
AU 2005203920	A1	20050721	AU 2005-203920		20050106
CA 2552726	A1	20050721	CA 2005-2552726		20050106
EP 1706402	A1	20061004	EP 2005-700246		20050106
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS					
CN 1910175	A	20070207	CN 2005-80002080		20050106
IN 2006DN04183	A	20070622	IN 2006-DN4183		20060720
PRIORITY APPLN. INFO.:			US 2004-534920P	P	20040108
			WO 2005-CA7	W	20050106

OTHER SOURCE(S): MARPAT 143:133700

GI



I



II

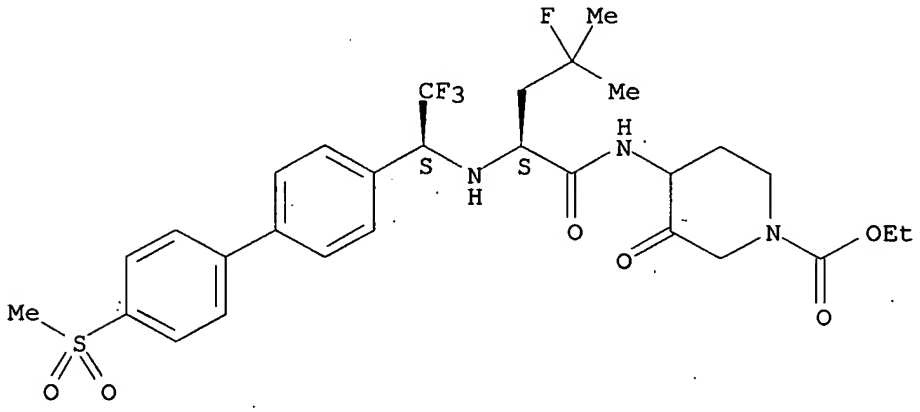
AB The invention relates to novel leucinamide derivs. I [X is (CR1R2)0-2; Y, Z are independently CR1R2, O, S, SO2, CO, NH or substituted imino; D, E are independently (un)substituted aryl or heteroaryl; n is 0 or 1; R1, R2 are independently H, halo or (un)substituted alkyl; or CR1R2 is a ring; R3 is alkyl or alkenyl; R4 is haloalkyl; R5 is H, alkyl, alkoxy, aryl, heteroaryl, cycloalkyl, heterocyclyl, OH, acyl, etc.] or their pharmaceutically-acceptable salts or stereoisomers, which are cathepsin cysteine protease inhibitors useful for treating and preventing cathepsin dependent conditions, e.g., osteoporosis, in which inhibition of bone resorption is indicated. Thus, peptide II was prepared by coupling of N-[(1S)-1-(4-bromophenyl)-2,2,2-trifluoroethyl]-4-fluoro-L-leucine with (4S,5R)-4-amino-5-methyldihydrofuran-3(2H)-one and [4-(methylthio)phenyl]boronic acid, followed by S-oxidation

IT 858945-60-5P 858945-61-6P 858945-62-7P
858945-63-8P 858945-64-9P 858945-65-0P
858945-66-1P 858945-67-2P 858945-68-3P
858945-69-4P 858945-70-7P 858945-71-8P
858945-72-9P 858945-73-0P 858945-74-1P

858945-75-2P 858945-76-3P 858945-80-9P
858945-81-0P 858945-82-1P 858945-83-2P
858945-84-3P 858945-85-4P 858945-86-5P
858945-87-6P 858945-88-7P 858945-89-8P
858945-90-1P 858945-91-2P 858945-92-3P
858945-93-4P 858945-94-5P 858945-95-6P
858945-96-7P 858945-97-8P 858945-98-9P
858945-99-0P 858946-00-6P 858946-02-8P
858946-04-0P 858946-06-2P 858946-08-4P
858946-10-8P 858946-12-0P 858946-14-2P
858946-16-4P 858946-19-7P 858946-22-2P
858946-24-4P 858946-26-6P 858946-28-8P
858946-30-2P 858946-32-4P 858946-34-6P
858946-36-8P 858946-39-1P 858946-41-5P
858946-42-6P 858946-45-9P 858946-46-0P
858946-48-2P 858946-50-6P 858946-51-7P
858946-54-0P 858946-56-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of peptides as cathepsin cysteine protease inhibitors)

RN 858945-60-5 ZCAPLUS
CN 1-Piperidinecarboxylic acid, 4-[[(2S)-4-fluoro-4-methyl-1-oxo-2-[[(1S)-2,2,2-trifluoro-1-[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]pentyl]amino]-3-oxo-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

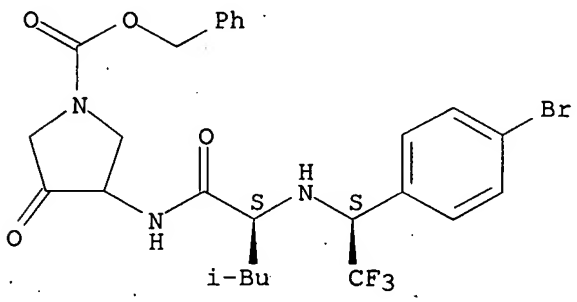


RN 858945-61-6 ZCAPLUS
CN 1-Pyrrolidinecarboxylic acid, 3-[[(2S)-4-fluoro-4-methyl-1-oxo-2-[[(1S)-2,2,2-trifluoro-1-[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]pentyl]amino]-4-oxo-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

CN 1-Pyrrolidinecarboxylic acid, 3-[[(2S)-2-[[(1S)-1-(4-bromophenyl)-2,2,2-trifluoroethyl]amino]-4-methyl-1-oxopentyl]amino]-4-oxo-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

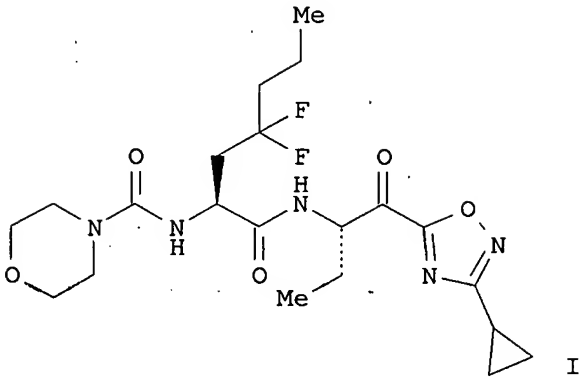


REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 16 OF 76 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:395290 ZCAPLUS
DOCUMENT NUMBER: 142:430533
TITLE: Preparation of novel peptide oxadiazole derivatives as cathepsin inhibitors
INVENTOR(S): Thurairatnam, Sukanthini; Aldous, David John; Leroy, Vincent; Timm, Andreas Paul
PATENT ASSIGNEE(S): Aventis Pharmaceuticals Inc., USA
SOURCE: PCT Int. Appl., 100 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005040142	A1	20050506	WO 2004-US35282	20041022
WO 2005040142	A9	20050609		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004284089	A1	20050506	AU 2004-284089	20041022
CA 2547591	A1	20050506	CA 2004-2547591	20041022
EP 1682524	A1	20060726	EP 2004-796294	20041022
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
BR 2004015826	A	20070102	BR 2004-15826	20041022
CN 1898219	A	20070117	CN 2004-80038912	20041022
JP 2007509175	T	20070412	JP 2006-536882	20041022
US 2006189657	A1	20060824	US 2006-409601	20060424
NO 2006002150	A	20060512	NO 2006-2150	20060512

PRIORITY APPLN. INFO.: US 2003-514373P P 20031024
WO 2004-US35282 W 20041022
OTHER SOURCE(S): CASREACT 142:430533; MARPAT 142:430533
GI



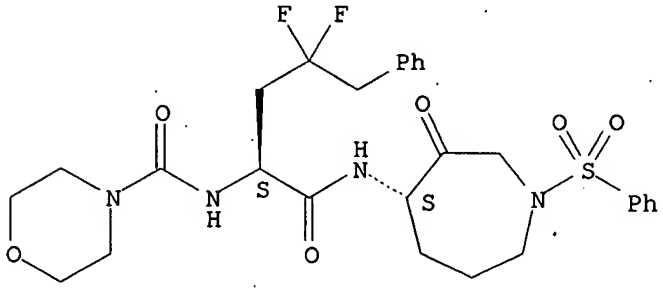
I

AB The invention relates to novel difluorinated amide derivs. R3NHCH(X1-CF2R2)CONR1R2 (X1 is CH2, CH2CH2 or a bond; R1-R4 are general substituents) and their pharmaceutically-acceptable salts and N-oxides which are inhibitors of cathepsin S, K, B, and L and includes their synthesis and use as therapeutic agents. Thus, peptide I was prepared by coupling intermediate amino acid derivs. (S)-4,4-difluoro-2-[(morpholine-4-carbonyl)amino]heptanoic acid with (S)-2-amino-1-(3-cyclopropyl-1,2,4-oxadiazol-5-yl)butan-1-ol hydrochloride in CH2Cl2 in the presence of diisopropylamine and PyBOP. The apparent inhibition consts. (Ki) for compds. of the invention, against cathepsin S, were in the range 10-10-10-7 M.

IT 850647-08-4P 850647-09-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of novel peptide oxadiazole derivs. as cathepsin inhibitors)

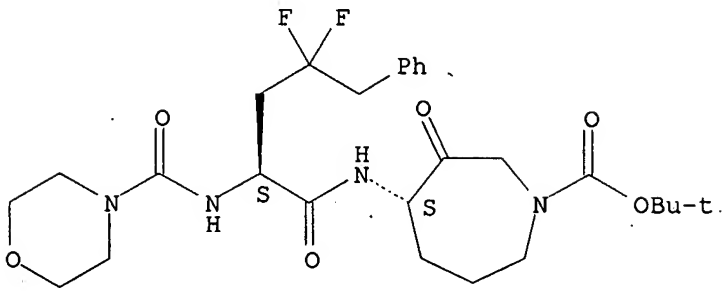
RN 850647-08-4 ZCAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-3,3-difluoro-1-[[[(4S)-hexahydro-3-oxo-1-(phenylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-4-phenylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 850647-09-5 ZCAPLUS
CN 1H-Azepine-1-carboxylic acid, 4-[[(2S)-4,4-difluoro-2-[(4-morpholinylcarbonyl)amino]-1-oxo-5-phenylpentyl]amino]hexahydro-3-oxo-, 1,1-dimethylethyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



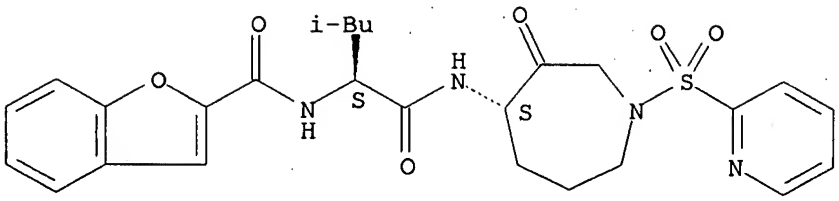
REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 17 OF 76 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:303283 ZCAPLUS
DOCUMENT NUMBER: 142:367703
TITLE: Methods for diagnosis and treatment of degenerative joint disease by regulating levels of cathepsin K, cathepsin S and tartarate-resistant acid phosphatase in dogs
INVENTOR(S): Muir, Peter; Vanderby, Ray; Provenzano, Paolo Pepe
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 45 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005074800	A1	20050407	US 2004-929919	20040830
CA 2438744	A1	20050228	CA 2003-2438744	20030829
PRIORITY APPLN. INFO.:			US 2003-499105P P	20030829

AB The present invention relates to methods for diagnosis and treatment of degenerative joint disease by regulating levels of cathepsin K, cathepsin S and tartarate-resistant acid phosphatase in dogs. The methods of diagnosis include determining increased expression of enzymes that are upregulated during the progress of joint and ligament inflammation and degeneration. In addition, disclosed are methods of treating the disease including inhibiting the activity of responsible proteases.
IT 281217-45-6, SB-357114
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods for diagnosis and treatment of degenerative joint disease by regulating levels of cathepsin K, cathepsin S and tartarate-resistant acid phosphatase in dogs)
RN 281217-45-6 ZCAPLUS
CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[(4S)-hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



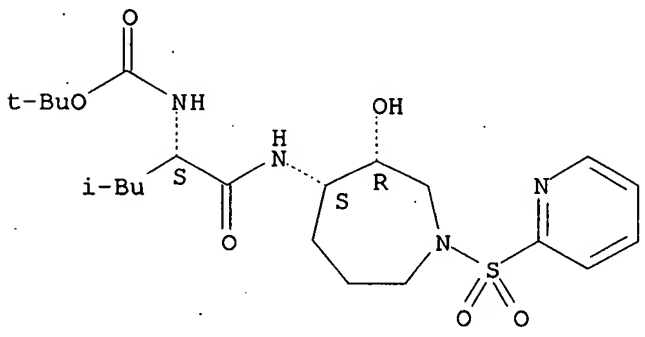
L4 ANSWER 18 OF 76 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:263672 ZCAPLUS
DOCUMENT NUMBER: 142:463586
TITLE: Asymmetric synthesis of a potent azepanone-based inhibitor of the cysteine protease cathepsin K
AUTHOR(S): Lee Trout, Robert E.; Marquis, Robert W.
CORPORATE SOURCE: Department of Medicinal Chemistry, Microbial, Musculoskeletal and Proliferative Diseases, GlaxoSmithKline, Collegeville, PA, 19426, USA
SOURCE: Tetrahedron Letters (2005), 46(16), 2799-2801
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 142:463586

AB In this account the asym. synthesis of a potent azepanone-based inhibitor of cathepsin K (Ki = 0.16 nM), which was shown to inhibit the production of biomarkers of bone resorption in monkeys was reported. The target compound was N-[(1S)-1-[[[(4S)-hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]-2-benzofurancarboxamide (SB 357114). The key steps in the synthesis sequence were the utility of the Evans aldol reaction coupled with the ring closing olefin metathesis to assemble the azepanone core contained within SB 357114.

IT 851815-73-1P 851815-74-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of (+)-N-[(S)-[[[(S)-hexa(hydro)(oxo)[(pyridinyl)sulfonyl]-1H-azepin-4-yl]amino]carbonyl][(methyl)butyl]-2-benzofurancarboxamide using Evans aldol reaction and ring closing olefin metathesis as key synthetic steps)

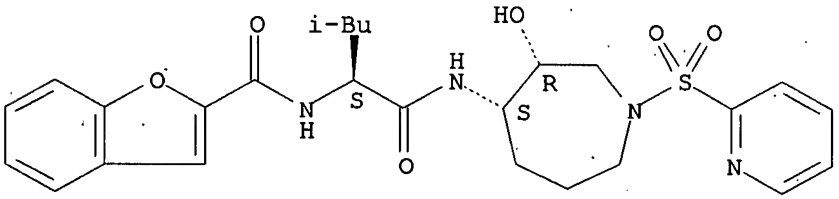
RN 851815-73-1 ZCAPLUS
CN Carbamic acid, [(1S)-1-[[[(3R,4S)-hexahydro-3-hydroxy-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



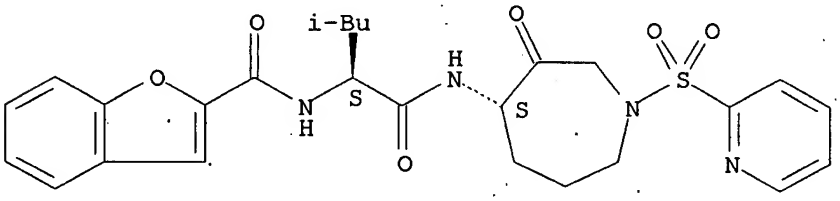
RN 851815-74-2 ZCAPLUS
CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[(3R,4S)-hexahydro-3-hydroxy-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 281217-45-6P, Benzofuran-2-carboxylic acid [(1S)-3-methyl-1-[[(4S)-3-oxo-1-(pyridine-2-sulfonyl)azepan-4-yl]carbamoyl]butyl]amide
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of (+)-N-[(S)-[[[(S)-hexa(hydro)(oxo)[(pyridinyl)sulfonyl]-1H-azepin-4-yl]amino]carbonyl][(methyl)butyl]-2-benzofurancarboxamide using Evans aldol reaction and ring closing olefin metathesis as key synthetic steps)
RN 281217-45-6 ZCAPLUS
CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[(4S)-hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 19 OF 76 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:219775 ZCAPLUS
DOCUMENT NUMBER: 142:280425
TITLE: Preparation of amino acid derivatives as cathepsin inhibitors
INVENTOR(S): Bayly, Christopher; Black, Cameron; McKay, Daniel J.
PATENT ASSIGNEE(S): Merck Frosst Canada & Co., Can.
SOURCE: PCT Int. Appl., 106 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

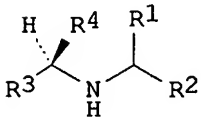
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005021487	A1	20050310	WO 2004-CA1577	20040823
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,				

GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
SN, TD, TG

AU 2004268707	A1	20050310	AU 2004-268707		20040823
CA 2535366	A1	20050310	CA 2004-2535366		20040823
EP 1660436	A1	20060531	EP 2004-761741		20040823
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK					
CN 1842515	A	20061004	CN 2004-80024520		20040823
JP 2007503401	T	20070222	JP 2006-524194		20040823
US 2006287402	A1	20061221	US 2006-569351		20060222
PRIORITY APPLN. INFO.:			US 2003-498017P	P	20030827
			WO 2004-CA1577	W	20040823

OTHER SOURCE(S): CASREACT 142:280425; MARPAT 142:280425

GI



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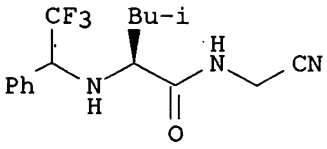


II

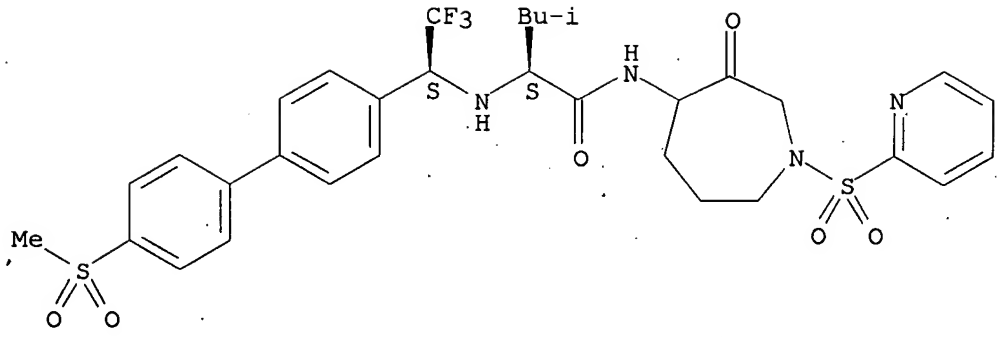
AB The invention relates to compds. I which are cysteine protease inhibitors, including but not limited to inhibitors of cathepsins K, L, S and B, and are useful for treating diseases in which inhibition of bone resorption is indicated, e.g., osteoporosis, osteoarthritis and rheumatoid arthritis. Thus, a mixture of L-leucine Me ester hydrochloride, 2,2,2-trifluoroacetophenone, diisopropylethylamine and TiCl4 in CH2Cl2 was stirred overnight, addnl. TiCl4 added, and the mixture stirred an addnl. 3 h. A solution of NaCNBH3 in MeOH was added and the mixture stirred 2 h to afford Me N-(2,2,2-trifluoro-1-phenylethyl)-L-leucinate. Saponification of the ester and reaction with aminoacetonitrile hydrochloride in DMF in the presence of PyBOP and Et3N yielded L-leucinamide derivative II.

IT 678982-29-1P 847361-59-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of amino acid derivs. as cathepsin inhibitors)

RN 678982-29-1 ZCAPLUS

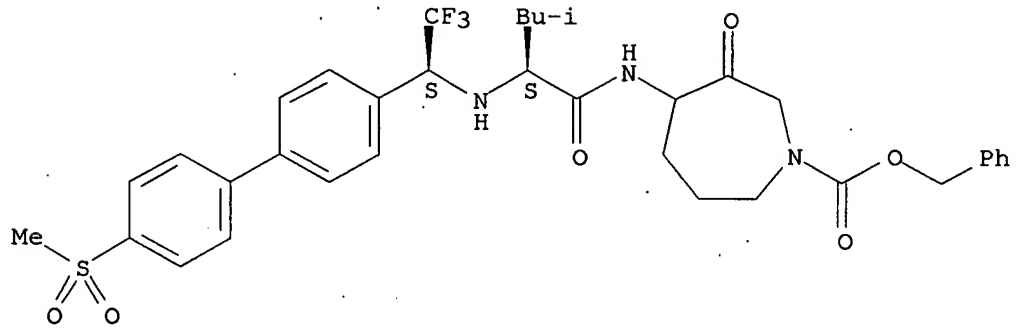
CN Pentanamide, N-[hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



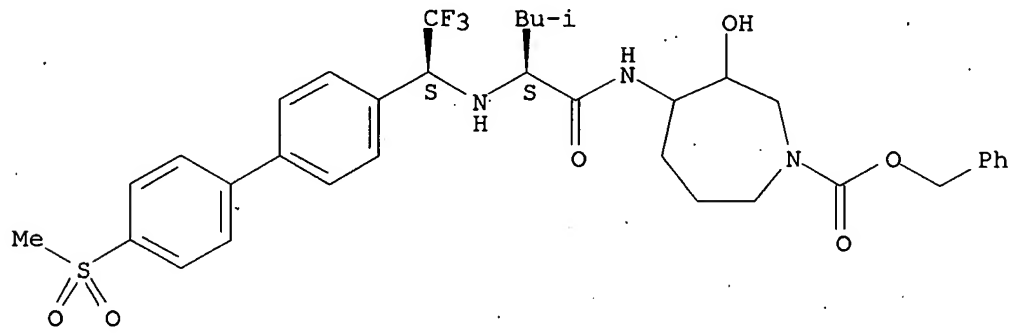
RN 847361-59-5 ZCAPLUS
CN 1H-Azepine-1-carboxylic acid, hexahydro-4-[[(2S)-4-methyl-1-oxo-2-[[(1S)-2,2,2-trifluoro-1-[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]pentyl]amino]-3-oxo-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



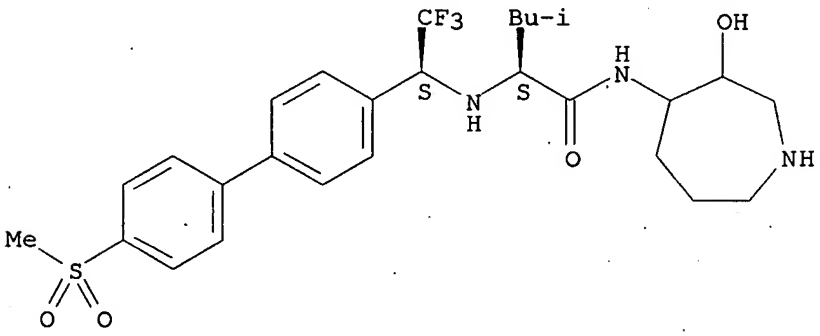
IT 678982-30-4P 678982-31-5P 847361-98-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of amino acid derivs. as cathepsin inhibitors)
RN 678982-30-4 ZCAPLUS
CN 1H-Azepine-1-carboxylic acid, hexahydro-3-hydroxy-4-[[(2S)-4-methyl-1-oxo-2-[[(1S)-2,2,2-trifluoro-1-[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]pentyl]amino]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



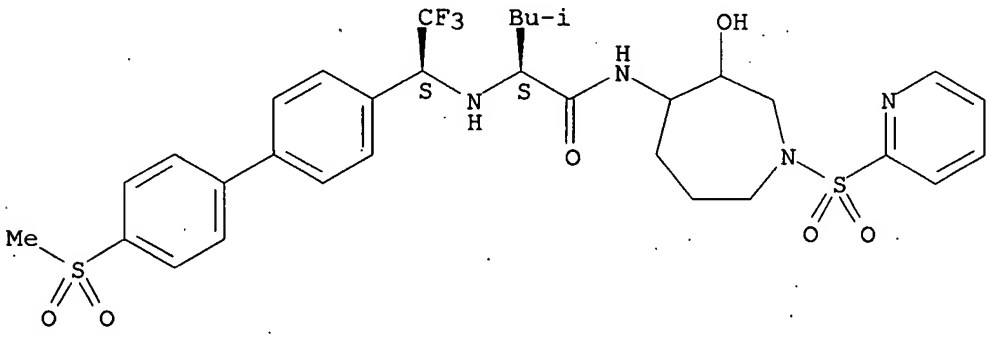
RN 678982-31-5 ZCAPLUS
CN Pentanamide, N-(hexahydro-3-hydroxy-1H-azepin-4-yl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 847361-98-2 ZCAPLUS
CN Pentanamide, N-[hexahydro-3-hydroxy-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 20 OF 76 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:138841 ZCAPLUS
DOCUMENT NUMBER: 142:240717
TITLE: Preparation of peptidyl 4-amino-3-azepanones as novel cathepsin K inhibitors
INVENTOR(S): Jeong, Jae U.
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2005013909	A2	20050217	WO 2004-US25645	20040804
WO 2005013909	A3	20050818		

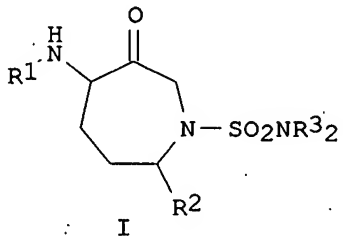
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-493314P P 20030807

OTHER SOURCE(S): CASREACT 142:240717; MARPAT 142:240717

GI



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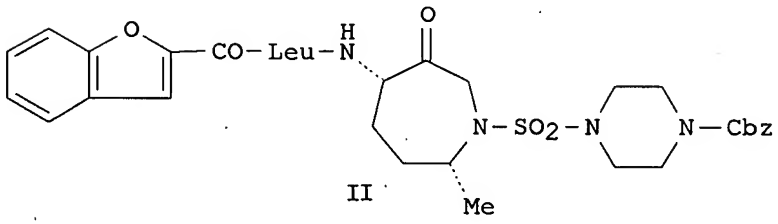


II

AB The invention relates to aminoazepanone derivs. I [R1 is an N-acyl amino acid moiety, including 1-aminocycloalkanecarboxylic acid residues; R2 is (un)substituted alkyl, alkenyl or alkynyl; R3 is independently H, (un)substituted alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl or heteroaryl or R32N is an (un)substituted nonarom. monocyclic ring] or their pharmaceutically-acceptable salts. Compds. I are protease inhibitors and can be useful in treating conditions in which the pathol. may be therapeutically modified by inhibiting a cysteine or serine protease of the papain superfamily, particularly cathepsin K. Thus, peptide II was prepared by a multistep sequence starting from (R)-Cbz-NHCHMeCH2OH (Cbz = benzyloxycarbonyl). The latter underwent iodination, reactions with allylmagnesium chloride and allyl bromide, and ring-closing metathesis to afford intermediate (R)-2-methyl-2,3,4,7-tetrahydro-1-azepanecarboxylic acid benzyl ester.

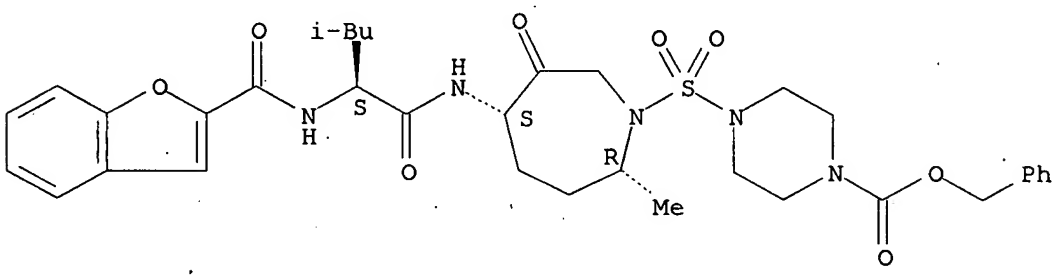
IT 844692-53-1P 844692-54-2P 844692-55-3P
844692-56-4P 844692-57-5P 844692-58-6P
844692-59-7P 844692-60-0P 844692-61-1P
844692-62-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

(Uses)
(preparation of peptidyl aminoazepanones as novel cathepsin K inhibitors)

RN 844692-53-1 ZCAPLUS

CN 1-Piperazinecarboxylic acid, 4-[[(2R,5S)-5-[[(2S)-2-[(2-benzofuranylcarbonyl)amino]-4-methyl-1-oxopentyl]amino]hexahydro-2-methyl-6-oxo-1H-azepin-1-yl]sulfonyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

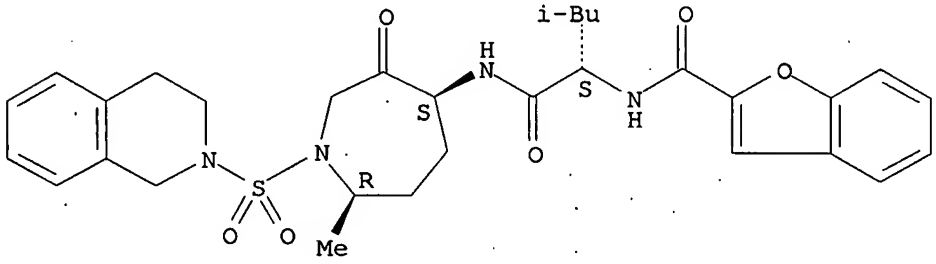
Absolute stereochemistry.



RN 844692-54-2 ZCAPLUS

CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[(4S,7R)-1-[(3,4-dihydro-2(1H)-isoquinolinyl)sulfonyl]hexahydro-7-methyl-3-oxo-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

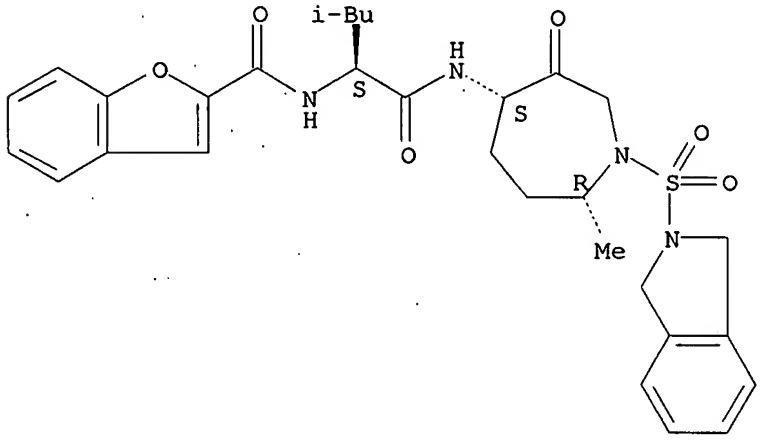
Absolute stereochemistry.



RN 844692-55-3 ZCAPLUS

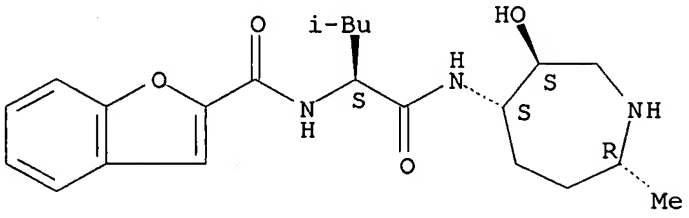
CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[(4S,7R)-1-[(1,3-dihydro-2H-isoindol-2-yl)sulfonyl]hexahydro-7-methyl-3-oxo-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



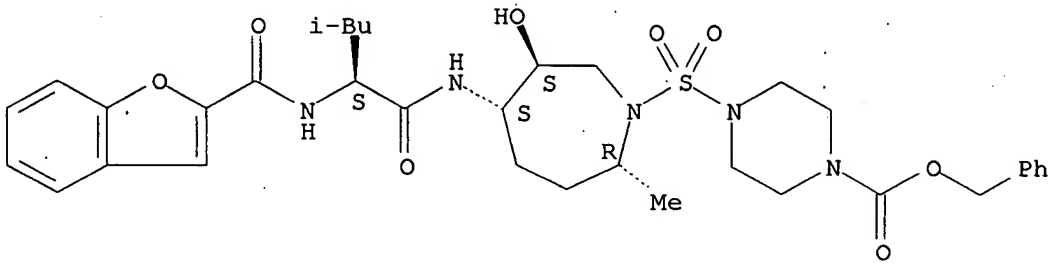
RN 844692-66-6 ZCAPLUS
CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[(3S,4S,7R)-hexahydro-3-hydroxy-7-methyl-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



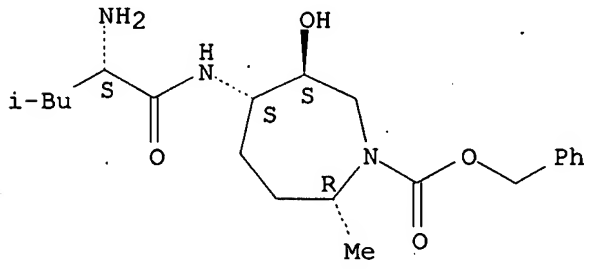
RN 844692-67-7 ZCAPLUS
CN 1-Piperazinecarboxylic acid, 4-[[(2R,5S,6S)-5-[[(2S)-2-[(2-benzofuranylcarbonyl)amino]-4-methyl-1-oxopentyl]amino]hexahydro-6-hydroxy-2-methyl-1H-azepin-1-yl]sulfonyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 881667-39-6 ZCAPLUS
CN 1H-Azepine-1-carboxylic acid, 5-[[(2S)-2-amino-4-methyl-1-oxopentyl]amino]hexahydro-6-hydroxy-2-methyl-, phenylmethyl ester, monohydrochloride, (2R,5S,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

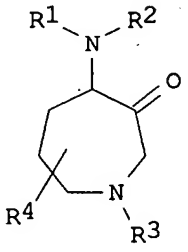
L4 ANSWER 21 OF 76 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:803931 ZCAPLUS
DOCUMENT NUMBER: 141:295878

10/ 789,063

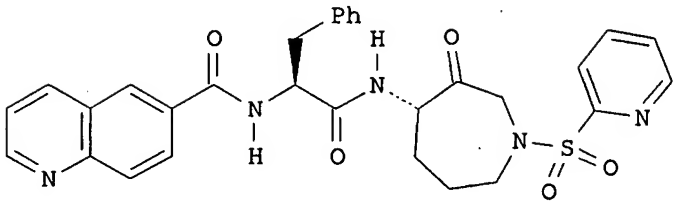
TITLE:	Preparation of aminoazepanones as Cathepsin L inhibitors
INVENTOR(S):	Marquis, Robert W.
PATENT ASSIGNEE(S):	USA
SOURCE:	U.S. Pat. Appl. Publ., 13 pp. CODEN: USXXCO
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1
PATENT INFORMATION:	

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2004192674	A1	20040930	US 2004-772817		20040205
PRIORITY APPLN. INFO.:			US 2003-447558P	P	20030214
OTHER SOURCE(S):	MARPAT 141:295878				

GI



I



II

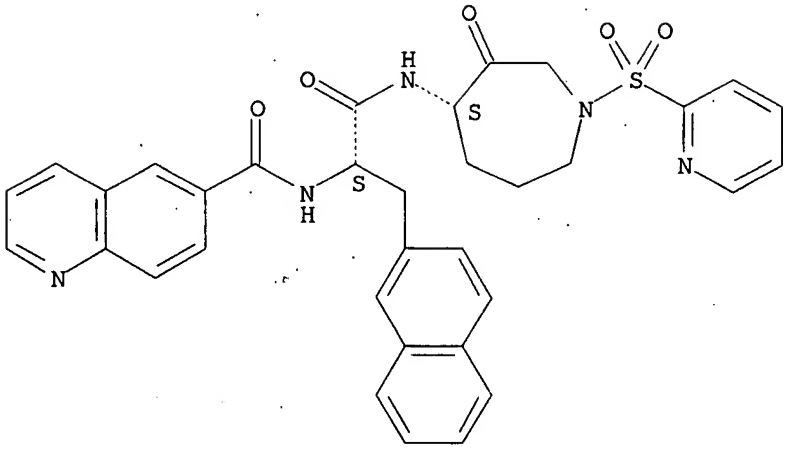
AB The title compds. I [R1 = substituted aminoalkylcarbonyl; R2 = H, alkyl, arylalkyl, etc.; R3 = H, alkyl, cycloalkyl, arylalkyl, etc.; R4 = H, alkyl, cycloalkyl, etc.] and their pharmaceutically acceptable salts are prepared and disclosed as inhibitors of Cathepsin L. Thus, e.g., II was prepared in a multistep synthesis employing N-Boc-phenylalanine. Consequently they are useful for preventing or treating diseases in which cathepsin L is implicated, such as rheumatoid arthritis or inhibition of pos. selection of CD4 + T-cells by cortical thymic epithelial cells.

IT 350796-38-2P 350796-41-7P 764650-55-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of aminoazepanones as inhibitors of Cathepsin L)

RN 350796-38-2 ZCAPLUS

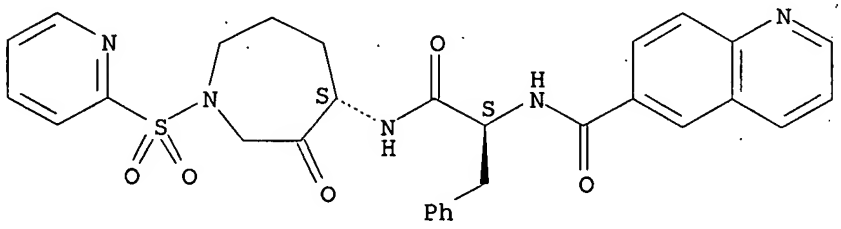
CN 6-Quinolinecarboxamide, N-[(1S)-2-[[(4S)-hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]-1-(2-naphthalenylmethyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



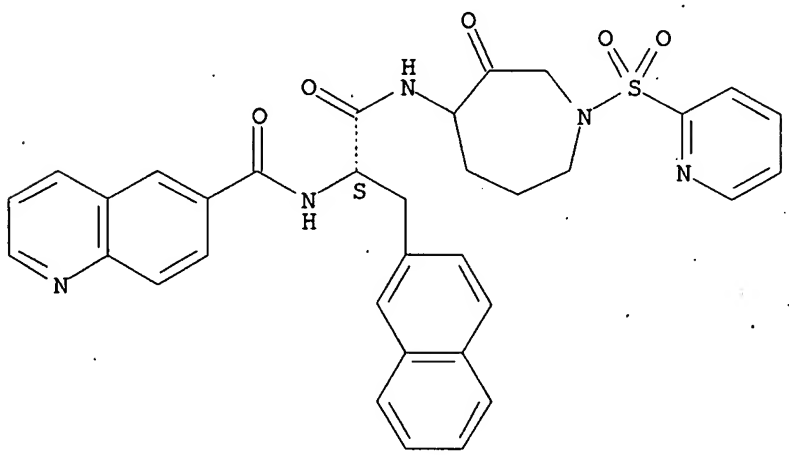
RN 350796-41-7 ZCAPLUS
CN 6-Quinolinecarboxamide, N-[(1S)-2-[[(4S)-hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]-2-oxo-1-(phenylmethyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 764650-55-7 ZCAPLUS
CN 6-Quinolinecarboxamide, N-[(1S)-2-[[hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]-1-(2-naphthalenylmethyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)

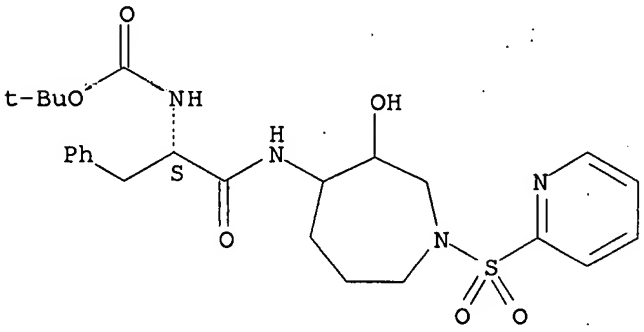
Absolute stereochemistry.



IT 369593-24-8P 369593-25-9P 764650-56-8P
764650-57-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of aminoazepanones as inhibitors of Cathepsin L)

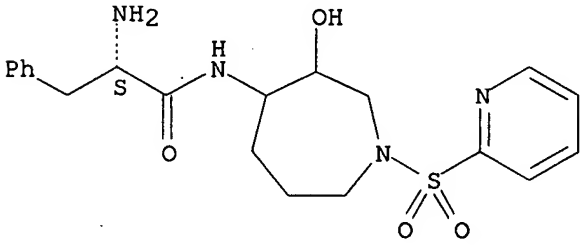
RN 369593-24-8 ZCAPLUS
CN Carbamic acid, [(1S)-2-[[hexahydro-3-hydroxy-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]-2-oxo-1-(phenylmethyl)ethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



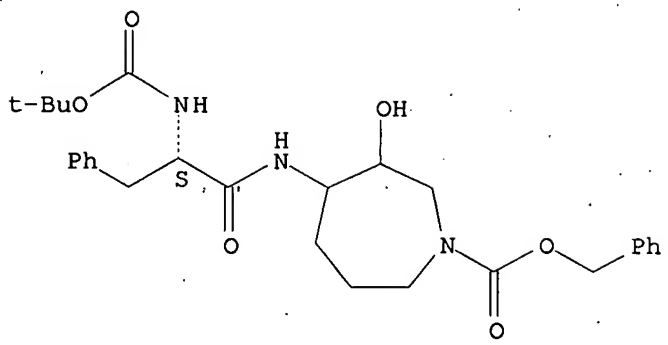
RN 369593-25-9 ZCAPLUS
CN Benzenepropanamide, α-amino-N-[hexahydro-3-hydroxy-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-, (αS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



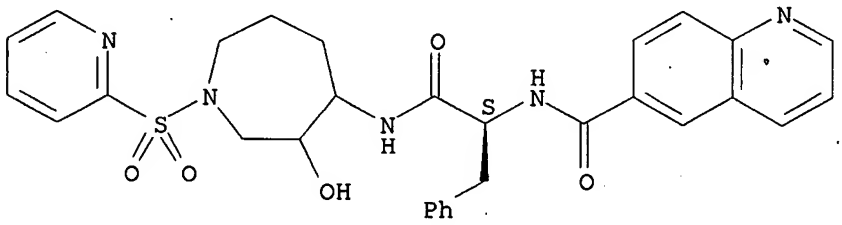
RN 764650-56-8 ZCAPLUS
CN 1H-Azepine-1-carboxylic acid, 4-[[(2S)-2-[[(1,1-dimethylethoxy)carbonyl]amino]-1-oxo-3-phenylpropyl]amino]hexahydro-3-hydroxy-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 764650-57-9 ZCAPLUS
CN 6-Quinolinecarboxamide, N-[(1S)-2-[[hexahydro-3-hydroxy-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]-2-oxo-1-(phenylmethyl)ethyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 22 OF 76 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:565073 ZCAPLUS
DOCUMENT NUMBER: 141:117186
TITLE: Use of cathepsin k inhibitors for the treatment of glaucoma
INVENTOR(S): Shepard, Allan; Clark, Abbot F.; Jacobson, Nasreen
PATENT ASSIGNEE(S): Alcon, Inc., Switz.
SOURCE: PCT Int. Appl., 57 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004058238	A1	20040715	WO 2003-US40511	20031219
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003297363	A1	20040722	AU 2003-297363	20031219

US 2006020001 A1 20060126 US 2005-537052 20050602
PRIORITY APPLN. INFO.: US 2002-436126P P 20021223
WO 2003-US40511 W 20031219

AB Compns. containing inhibitors of cathepsin K (CTSK) expression and/or activity are provided. Methods for the treatment of glaucoma using the compns. of the invention are further provided. The cathepsin K antagonist is selected from, but not limited to, the group consisting of monensin, brefeldin A, tunicamycin and 1,3-bis(acylamino)-2-propanone derivs., cycloaltilisin 6, cycloaltilisin 7, AC-3-1, AC-3-3, AC-5-1, haploscleridamine, SB-331750, SB-357114, peptidomimetic aminomethyl ketones, α,α'-diacylamino ketones, alkoxymethyl ketones, cyanamides, pyridoxal propionate derivs. (including Clik-164 and Clik-166), SB-290190, α-alkoxy ketone derivs., cyanamide derivs., and Nα-acyl-α-amino acid-(arylaminoethyl)amides.

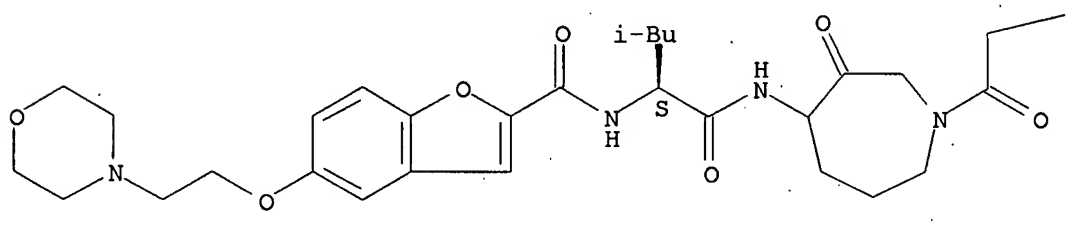
IT 486442-96-0, SB 331750
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(SB 331750; use of cathepsin k inhibitors for treatment of glaucoma)

RN 486442-96-0 ZCAPLUS

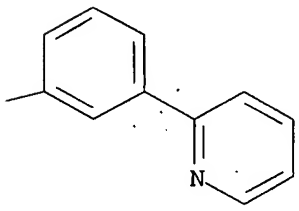
CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[hexahydro-3-oxo-1-[[3-(2-pyridinyl)phenyl]acetyl]-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]-5-[2-(4-morpholinyl)ethoxy]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Currently available stereo shown.

PAGE 1-A



PAGE 1-B

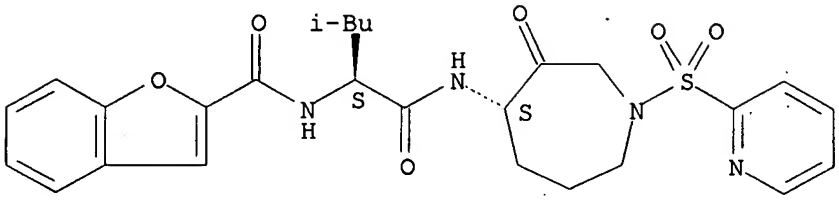


IT 281217-45-6, SB-357114
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of cathepsin k inhibitors for treatment of glaucoma)

RN 281217-45-6 ZCAPLUS

CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[(4S)-hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 23 OF 76 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:500870 ZCAPLUS
DOCUMENT NUMBER: 142:16826
TITLE: Medicine for treating obesity, diabetes mellitus and related diseases
INVENTOR(S): Chen, Jingming; Yong, Heng
PATENT ASSIGNEE(S): Shen, Aifu, Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 62 pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

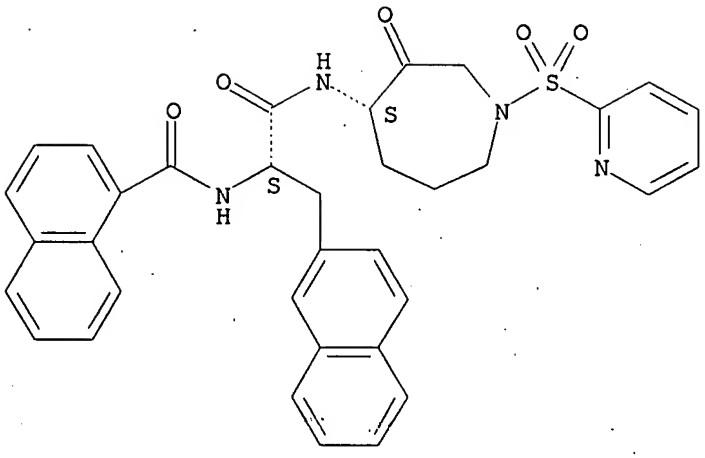
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1400018	A	20030305	CN 2001-123953	20010808

PRIORITY APPLN. INFO.: CN 2001-123953 20010808

AB The application of the inhibitors of cathepsins L, K, and S for treating obesity, diabetes mellitus, and their related diseases (such as hyperinsulina, hyperglycemia, hypertension, heart diseases, infecundity, etc.) is presented. The inhibitors of cathepsins L, K, and S are antisense sequence of human cathepsin L cDNA or its un-translated region at 5' end, anti-cathepsin L antibody, cystatin C mutant, saxiphilin, precursor of cathepsin L, epoxysuccinate derivative lowering the activity of cathepsin L, aziridine-2,3-dicarboxylate derivative or peptide aldehyde derivative
inhibiting the activity of cathepsin L, or dipeptide hydroxy-amidic acid ester derivative or sulfonyl derivative inhibiting the activity of cathepsin L.

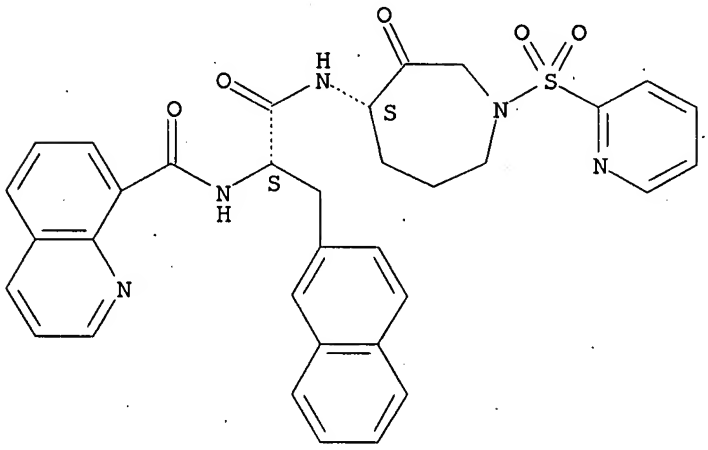
IT 350796-39-3P 773858-03-0P 773858-08-5P
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(medicine for treating obesity diabetes mellitus and related diseases)
RN 350796-39-3 ZCAPLUS
CN 2-Naphthalenepropanamide, N-[(4S)-hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-α-[(1-naphthalenylcarbonyl)amino]-, (αS)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



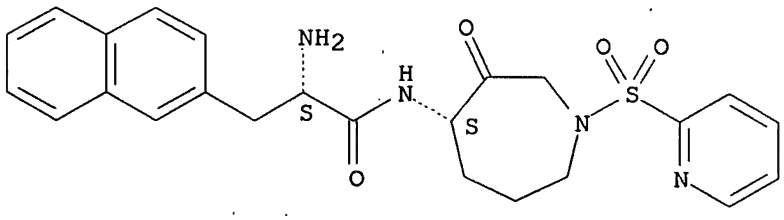
RN 773858-03-0 ZCAPLUS
CN 8-Quinolinecarboxamide, N-[(1S)-2-[[(4S)-hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]-1-(2-naphthalenylmethyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 773858-08-5 ZCAPLUS
CN 2-Naphthalenepropanamide, α-amino-N-[(4S)-hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-, (αS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

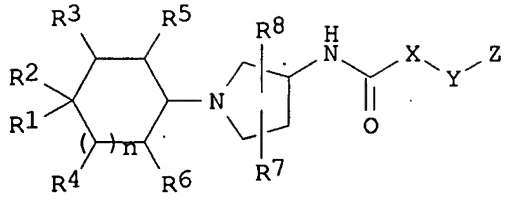


L4 ANSWER 24 OF 76 ZCAPLUS COPYRIGHT 2007 ACS on STN

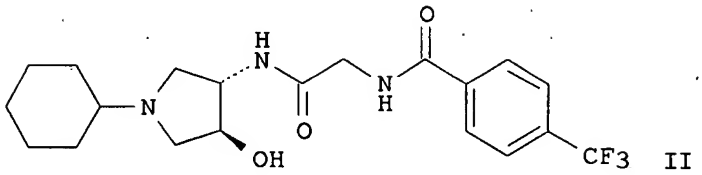
ACCESSION NUMBER: 2004:486379 ZCAPLUS
DOCUMENT NUMBER: 141:54188
TITLE: Preparation of 3-aminopyrrolidine chemokine receptor antagonists as antiinflammatory and immunomodulatory bioactive compounds
INVENTOR(S): Xue, Chu-Biao; Metcalf, Brian; Feng, Hao; Cao, Ganfeng; Huang, Taishing; Zheng, Changsheng; Robinson, Darius J.; Han, Amy Qi
PATENT ASSIGNEE(S): Incyte Corporation, USA
SOURCE: PCT Int. Appl., 221 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004050024	A2	20040617	WO 2003-US37946		20031126
WO 2004050024	A3	20040729			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW					
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2507501	A1	20040617	CA 2003-2507501		20031126
AU 2003293129	A1	20040623	AU 2003-293129		20031126
EP 1565436	A2	20050824	EP 2003-790120		20031126
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
BR 2003016732	A	20051018	BR 2003-16732		20031126
CN 1741994	A	20060301	CN 2003-80109198		20031126
JP 2006516145	T	20060622	JP 2004-570963		20031126
SE 2005001185	A	20050707	SE 2005-1185		20050526
NO 2005002543	A	20050722	NO 2005-2543		20050526
ZA 2005004322	A	20060222	ZA 2005-4322		20050526
IN 2005KN01051	A	20060630	IN 2005-KN1051		20050602
US 2006252751	A1	20061109	US 2006-535795		20060421
PRIORITY APPLN. INFO.:			US 2002-429605P	P	20021127
			US 2003-463976P	P	20030418
			WO 2003-US37946	W	20031126

OTHER SOURCE(S): MARPAT 141:54188
GI



I



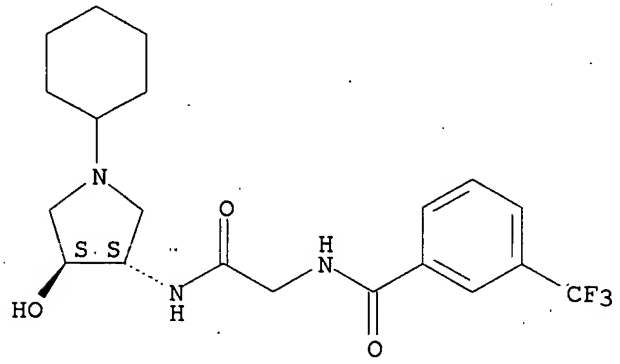
II

AB Title compds. I [wherein X = (un)substituted (hetero)aryl, (cyclo)alkyl; Y = a bond, O, S, NH, NHCO, NHCS, NHSO2, CO, CHOH, CH(O-alkyl), NOH, NHCONH; Z = (un)substituted cycloalkyl, (hetero)aryl, heterocyclyl; R1 = independently (un)substituted cycloalkyl, heterocyclyl, (hetero)aryl(alkyl), (hetero)arylalkenyl, (hetero)arylalkynyl, (hetero)arylaminocarbonyl, (hetero)arylcarboxamido, (hetero)arylureido, (hetero)aryloxy, (hetero)arylamino; R2 = independently H, OH, (esterified) carboxyl, CN, (cyclo)alkyl, (cyclo)alkenyl, alkynyl, alkoxy, thioalkyl, haloalkyl, halo, (hetero)aryl, (un)substituted amino, carboxamido; or CR1R2 = spirocycle; R3-R6 = independently H, NH2, OH, (halo)alkyl ,alkenyl, alkynyl, (hetero)aryl(alkyl), alkoxy, thioalkyl; or C2R1R3 = (un)substituted carbocycle, heterocycle; or R3 and R4 or R5 and R6 join to form a bridged bicyclic system having an ethylene bridge; or R3 and R6 join to form a bicyclic system having a methylene, ethylene, or heteroatom bridge; R7 and R8 = independently, H, alkyl optionally interrupted by O or S, alkoxy(alkyl), haloalkyl, (hetero)aryloxy(alkyl); or R7 and R8 join to form a spircarbocycle or spiroheterocycle; n = 0-3; and enantiomers, diastereomers, prodrugs, solvates, metabolites, and pharmaceutically acceptable salts thereof] were prepared as modulators of chemokine receptor activity, particularly of the CCR2 and/or CCR5 (no data) receptors. For example, coupling of glycine Me ester hydrochloride and 3-(trifluoromethyl)benzoyl chloride using TEA in H2O and THF gave (3-trifluoromethylbenzoylamino)acetic acid, which was amidated with tert-Bu (3S,4S)-3-amino-4-hydroxypyrrolidine-1-carboxylate (3-step preparation given) using TEA and BOP in DMF. N-deprotecting with TFA in CH2Cl2, followed by alkylation with cyclohexanone using TEA and Na(OAc)3BH in THF provided the N-[2-(pyrrolidinylamino)-2-oxoethyl]benzamide II. In CCR2 specific binding assays using peripheral blood mononuclear cells (PBMCs) derived from normal human whole blood, compds. of the invention exhibited antagonist activity with IC50 values ranging from about 0.01 nM to about 500 nM. In addition, compds. of the invention demonstrated CCR2 antagonist activity by inhibiting MCP-1 induced leukocyte chemotaxis in human PBMCs with IC50 values ranging from about 1 nM to about 3000 nM. Thus, I and their compns. are useful for treating diseases associated with chemokine activity, such as atherosclerosis, restenosis, lupus, organ transplant rejection, and rheumatoid arthritis (no data).

IT 708273-17-0P, N-[2-[((3S,4S)-1-Cyclohexyl-4-hydroxypyrrolidin-3-yl)amino]-2-oxoethyl]-3-(trifluoromethyl)benzamide 709018-11-1P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(CCR2 antagonist; preparation of aminopyrrolidine CCR2 antagonists as

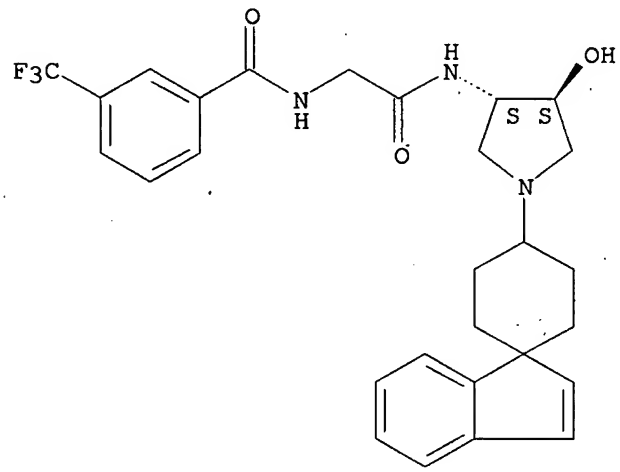
antiinflammatory agents and immunomodulators)
RN 708273-17-0 ZCAPLUS
CN Benzamide, N-[2-[[(3S,4S)-1-cyclohexyl-4-hydroxy-3-pyrrolidinyl]amino]-2-oxoethyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 709018-11-1 ZCAPLUS
CN Benzamide, N-[2-[(4-hydroxy-1-spiro[cyclohexane-1,1'-[1H]inden]-4-yl-3-pyrrolidinyl)amino]-2-oxoethyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

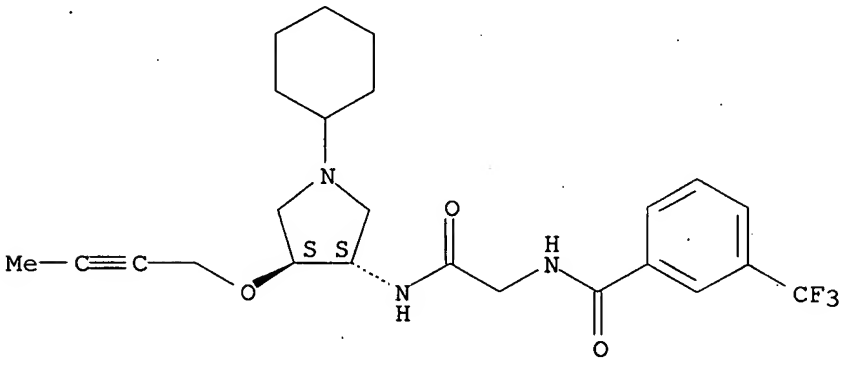


IT 708273-18-1P 708273-19-2P 708273-21-6P
708273-22-7P 709017-20-9P 709017-22-1P
709017-24-3P 709017-26-5P 709017-28-7P
709017-30-1P 709017-32-3P 709017-34-5P
709017-36-7P 709017-38-9P 709017-41-4P
709017-43-6P 709017-45-8P 709017-47-0P
709017-49-2P 709017-51-6P 709017-53-8P
709017-55-0P 709017-57-2P 709017-59-4P
709017-61-8P 709017-63-0P 709017-65-2P
709017-67-4P 709017-69-6P 709017-71-0P
709017-73-2P 709017-75-4P 709017-77-6P
709017-79-8P 709017-81-2P 709017-83-4P
709017-85-6P 709017-87-8P 709017-89-0P
709017-91-4P 709017-93-6P 709017-95-8P

709017-97-0P 709017-99-2P 709018-01-9P
709018-03-1P 709018-05-3P 709018-07-5P
709018-09-7P 709018-13-3P 709018-17-7P
709018-19-9P 709018-21-3P 709018-23-5P
709018-25-7P 709018-27-9P 709018-29-1P
709018-31-5P 709018-33-7P 709018-35-9P
709018-37-1P 709018-39-3P 709018-41-7P
709018-43-9P 709018-46-2P 709018-49-5P
709018-52-0P 709018-55-3P 709018-58-6P
709018-61-1P 709018-64-4P 709018-66-6P
709018-69-9P 709018-72-4P 709018-74-6P
709018-77-9P 709018-79-1P 709018-81-5P
709018-84-8P 709018-86-0P 709018-88-2P
709018-90-6P 709018-92-8P 709018-94-0P
709018-96-2P 709018-98-4P 709019-00-1P
709019-02-3P 709019-04-5P 709019-06-7P
709019-08-9P 709019-10-3P 709019-12-5P
709019-14-7P 709019-16-9P 709019-18-1P
709019-20-5P 709019-22-7P 709019-24-9P
709019-26-1P 709019-28-3P 709019-30-7P
709019-32-9P 709019-34-1P 709019-36-3P
709019-38-5P 709019-40-9P 709019-42-1P
709019-44-3P 709019-46-5P 709024-42-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(CCR2 antagonist; preparation of aminopyrrolidine CCR2 antagonists as antiinflammatory agents and immunomodulators)

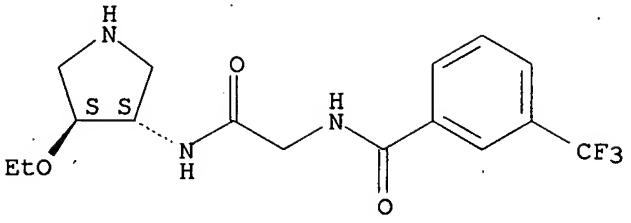
RN 708273-18-1 ZCAPLUS
CN Benzamide, N-[2-[[(3S,4S)-4-(2-butynyloxy)-1-cyclohexyl-3-pyrrolidinyl]amino]-2-oxoethyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



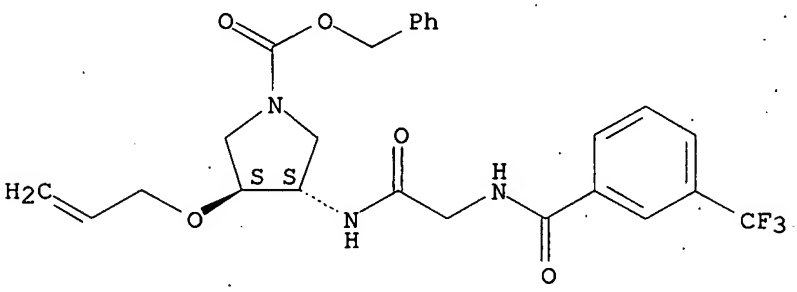
RN 708273-19-2 ZCAPLUS
CN Benzamide, N-[2-[[(3S,4S)-1-cyclohexyl-4-(phenylmethoxy)-3-pyrrolidinyl]amino]-2-oxoethyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



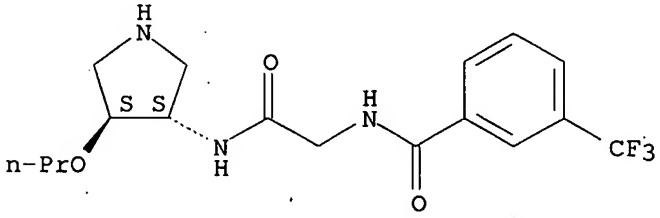
RN 708273-53-4 ZCAPLUS
CN 1-Pyrrolidinecarboxylic acid, 3-(2-propenyloxy)-4-[[[[3-(trifluoromethyl)benzoyl]amino]acetyl]amino]-, phenylmethyl ester, (3S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 708273-54-5 ZCAPLUS
CN Benzamide, N-[2-oxo-2-[[(3S,4S)-4-propoxy-3-pyrrolidinyl]amino]ethyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

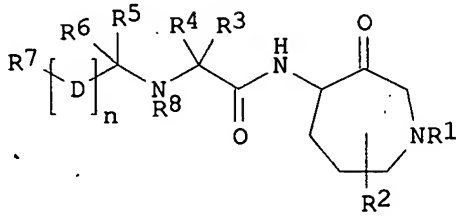


L4 ANSWER 25 OF 76 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:333709 ZCAPLUS
DOCUMENT NUMBER: 140:321727
TITLE: Preparation of 4-aminoazepan-3-one peptides as cathepsin K inhibitors useful in the treatment of osteoporosis
INVENTOR(S): Black, Cameron
PATENT ASSIGNEE(S): Merck Frosst Canada & Co., Can.
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004033445	A1	20040422	WO 2003-CA1551	20031007
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2500317	A1	20040422	CA 2003-2500317	20031007
AU 2003273697	A1	20040504	AU 2003-273697	20031007
EP 1551823	A1	20050713	EP 2003-757604	20031007
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2006504719	T	20060209	JP 2004-542127	20031007
US 2006166966	A1	20060727	US 2005-530250	20050405
PRIORITY APPLN. INFO.:			US 2002-416892P	P 20021008
			WO 2003-CA1551	W 20031007

OTHER SOURCE(S): MARPAT 140:321727

GI



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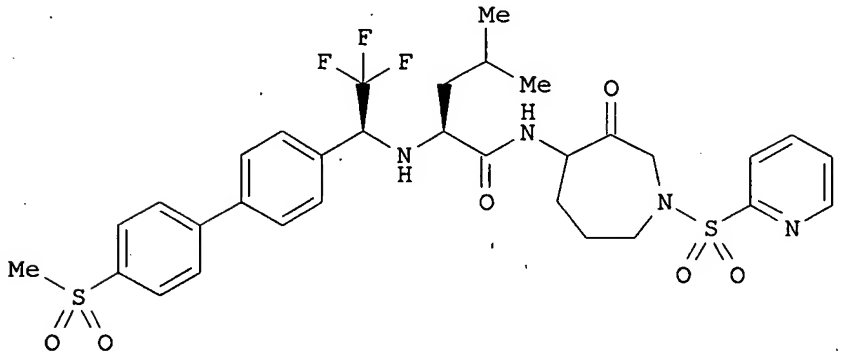


II

AB The invention relates to azepinones I [R1 is H, alkyl, a sulfonyl or acyl group, arylalkyl; R2 is H or (cyclo)alkyl; R3 is H, alk(en)yl, haloalk(en)yl or cycloalk(en)yl; or R3R4C is (un)substituted (hetero)cycloalk(en)yl; R5 is H, alkyl or haloalkyl; R6 is haloalkyl, (un)substituted (hetero)aryl or (hetero)arylalkyl; R7 is H, alk(en)(yn)yl, alkoxy, halo, nitro, cyano, (hetero)aryl, carboxy, etc.; D is (un)substituted alk(en)ylene or (hetero)arylene; n is 0-3] or their pharmaceutically-acceptable salts, stereoisomers and N-oxides which are

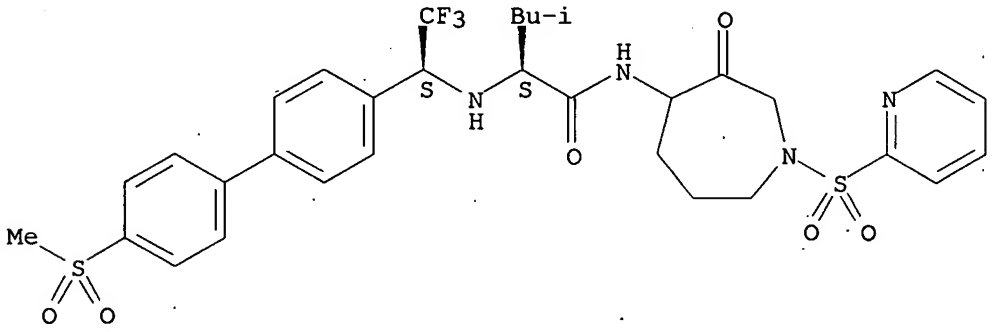
cysteine protease inhibitors, in particular, inhibitors of cathepsins K, L, S and B. These compds. are useful for treating diseases, e.g., osteoporosis, in which inhibition of bone resorption is indicated. Thus, aminoazepanone peptide II was prepared by a multistep procedure starting with reaction of silyl-protected L-leucinol with trifluoroacetaldehyde Me hemiacetal.

IT 678982-29-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of aminoazepanone peptides as cathepsin K inhibitors for treatment of osteoporosis)

RN 678982-29-1 ZCAPLUS

CN Pentanamide, N-[hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

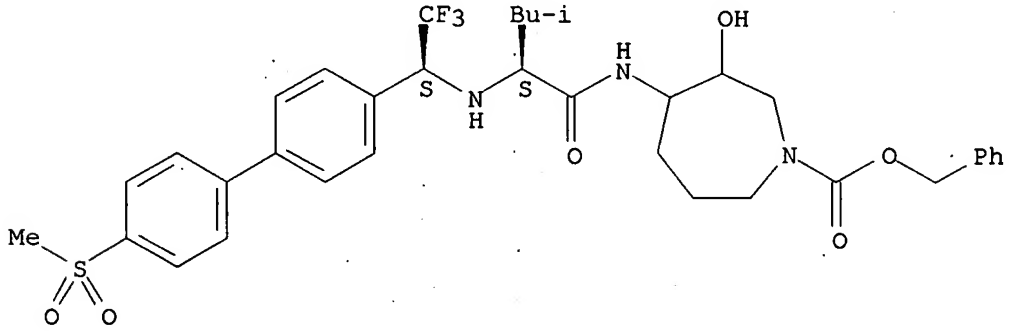


IT 678982-30-4P 678982-31-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of aminoazepanone peptides as cathepsin K inhibitors for treatment of osteoporosis)

RN 678982-30-4 ZCAPLUS

CN 1H-Azepine-1-carboxylic acid, hexahydro-3-hydroxy-4-[[(2S)-4-methyl-1-oxo-2-[[(1S)-2,2,2-trifluoro-1-[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]pentyl]amino]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

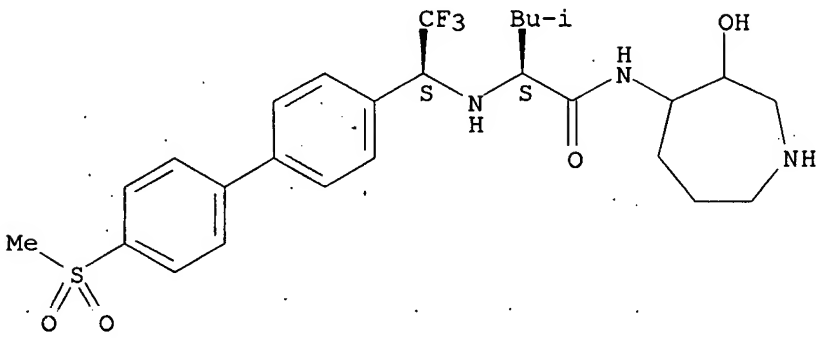


RN 678982-31-5 ZCAPLUS

CN Pentanamide, N-(hexahydro-3-hydroxy-1H-azepin-4-yl)-4-methyl-2-[[(1S)-

2,2,2-trifluoro-1-[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

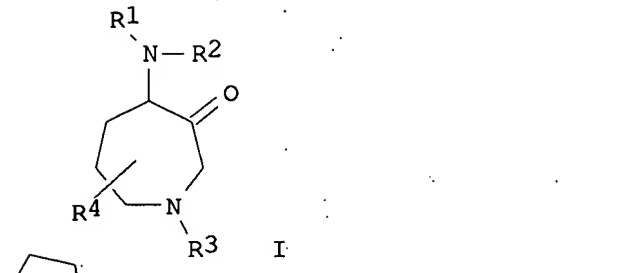


REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

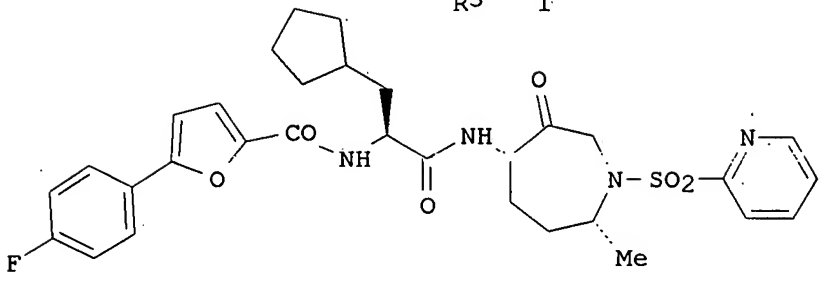
L4 ANSWER 26 OF 76 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:182661 ZCAPLUS
DOCUMENT NUMBER: 140:235616
TITLE: Preparation of 4-amino-azepan-3-ones as cathepsin S inhibitors
INVENTOR(S): Bondinell, William E.; Hall, Ralph F.; Jin, Qi; Kerns, Jeffrey K.; Nie, Hong; Widdowson, Katherine L.
PATENT ASSIGNEE(S): SmithKline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 83 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004017911	A2	20040304	WO 2003-US26358	20030822
WO 2004017911	A3	20040701		
W: AE, AG, AL, AU, BA, BB, BR, BZ, CA, CN, CO, CR, CU, DM, DZ, EC, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, OM, PH, PL, RO, SC, SG, TN, TT, UA, US, UZ, VN, YU, ZA				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003269984	A1	20040311	AU 2003-269984	20030822
EP 1539178	A2	20050615	EP 2003-751880	20030822
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2006505526	T	20060216	JP 2004-529860	20030822
US 2006052365	A1	20060309	US 2005-525114	20050927
PRIORITY APPLN. INFO.:			US 2002-405227P	P 20020822
			WO 2003-US26358	W 20030822

OTHER SOURCE(S): MARPAT 140:235616
GI



I



II

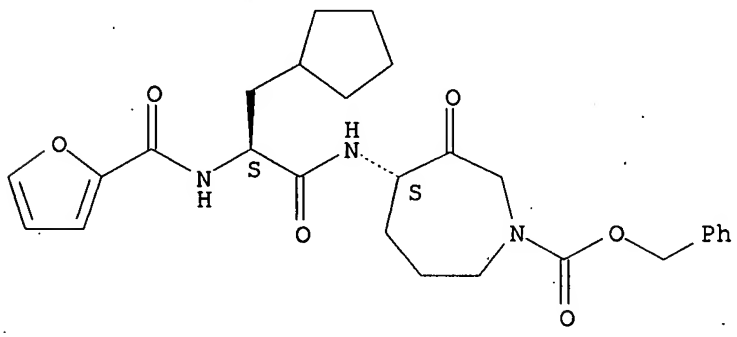
AB 4-Amino-azepan-3-ones of formula I [R1 = (substituted) aminomethylcarbonyl, acyl, etc.; R2 = H, alkyl, arylalkyl, etc.; R3 = H, alkyl, cycloalkyl-alkyl, acyl, etc.; R4 = alkyl, etc.] are prepared The compds. are useful as protease inhibitors, particularly of cathepsin S, and as such are useful for preventing a number of diseases amongst which are atherosclerotic lesions and pulmonary diseases such as asthma and allergic reactions (no data). Thus, II was prepared from 4-fluorophenylboronic acid and 5-bromofuran-2-carboxylic acid [(S)-2-cyclopentyl-1-[(4S,7R)-7-methyl-3-oxo-1-(pyridin-2-sulfonyl)-azepan-4-ylcarbamoyl]-ethyl]-amide (preparation given) in 24% yield.

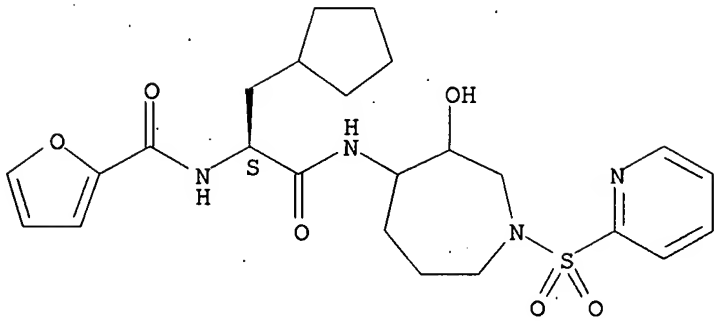
IT 666725-65-1P 666725-66-2P 666725-67-3P
666725-68-4P 666725-69-5P 666725-70-8P
666725-71-9P 666725-72-0P 666725-73-1P
666725-74-2P 666725-75-3P 666725-76-4P
RL: PAC (Pharmacological activity); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of amino-azepanones as cathepsin S inhibitors)

RN 666725-65-1 ZCAPLUS

CN 1H-Azepine-1-carboxylic acid, 4-[[(2S)-3-cyclopentyl-2-[(2-furanylcarbonyl)amino]-1-oxopropyl]amino]hexahydro-3-oxo-, phenylmethyl ester, (4S)- (9CI) (CA INDEX NAME)

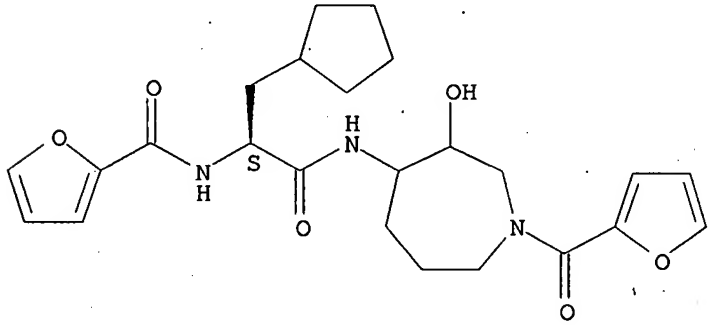
Absolute stereochemistry.





RN 666726-23-4 ZCAPLUS
CN 2-Furancarboxamide, N-[(1S)-1-(cyclopentylmethyl)-2-[[1-(2-furanylcarbonyl)hexahydro-3-hydroxy-1H-azepin-4-yl]amino]-2-oxoethyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 27 OF 76 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:142902 ZCAPLUS
DOCUMENT NUMBER: 140:187404
TITLE: Electrospun amorphous pharmaceutical compositions
INVENTOR(S): Ignatious, Francis; Sun, Linghong
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004014304	A2	20040219	WO 2003-US24641	20030807
WO 2004014304	A3	20040624		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,

BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2494865	A1	20040219	CA 2003-2494865	20030807
AU 2003258120	A1	20040225	AU 2003-258120	20030807
EP 1534250	A2	20050601	EP 2003-784959	20030807
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003013222	A	20050614	BR 2003-13222	20030807
CN 1684673	A	20051019	CN 2003-823237	20030807
JP 2005534716	T	20051117	JP 2004-527797	20030807
US 2006013869	A1	20060119	US 2005-523835	20050207
US 2006083784	A1	20060420	US 2005-64890	20050224
NO 2005001123	A	20050506	NO 2005-1123	20050302

PRIORITY APPLN. INFO.:

US 2002-401726P	P	20020807
WO 2003-US24641	W	20030807
US 2005-523835	A2	20050207

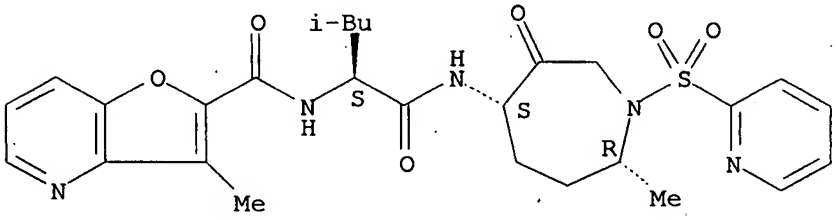
AB The present invention is directed to use of electrospinning, i.e. the process of making polymer nanofibers from either a solution or melt under elec. forces, to prepare stable, solid dispersions of amorphous drugs in polymer nanofibers. Thus, carvedilol-HBr monohydrate wa dissolved in THF and water. The solution was added to Polyox WSR1105 in MeCN solution This solution was spun to give nanofibers, and the morphol. of the drug was shown to be amorphous.

IT 362505-94-0
RL: PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(electrospun amorphous pharmaceutical compns.)

RN 362505-94-0 ZCAPLUS

CN Furo[3,2-b]pyridine-2-carboxamide, N-[(1S)-1-[[[(4S,7R)-hexahydro-7-methyl-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]-3-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 28 OF 76 ZCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:	2003:1007855 ZCAPLUS
DOCUMENT NUMBER:	140:59456
TITLE:	Preparation of sterically-awkward β-lactam derivatives as β-lactamase inhibitors
INVENTOR(S):	Shoichet, Brian K.; Blaszczak, Larry C.
PATENT ASSIGNEE(S):	USA
SOURCE:	U.S. Pat. Appl. Publ., 22 pp. CODEN: USXXCO
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	2
PATENT INFORMATION:	

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

US 2003236243	A1	20031225	US 2003-438280	20030514
WO 2004037163	A2	20040506	WO 2003-US15140	20030514
WO 2004037163	A3	20050224		

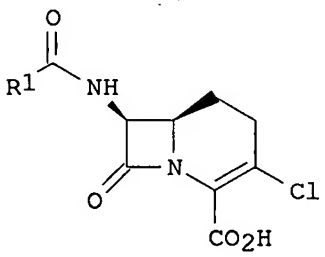
W: AU, CA, CN, JP
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR

AU 2003298513	A1	20040513	AU 2003-298513	20030514
US 2005245498	A1	20051103	US 2005-83151	20050317

PRIORITY APPLN. INFO.:
US 2002-380411P P 20020514
US 2003-438280 A2 20030514
WO 2003-US15140 W 20030514

OTHER SOURCE(S): MARPAT 140:59456

GI



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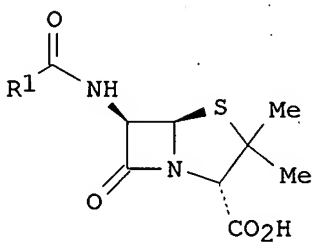
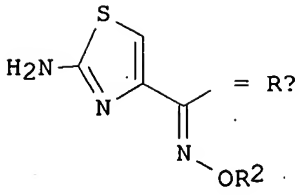
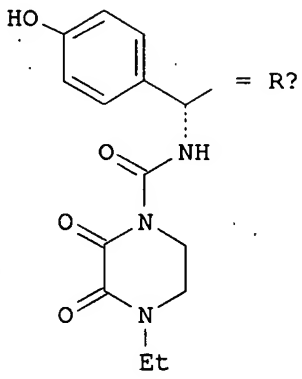
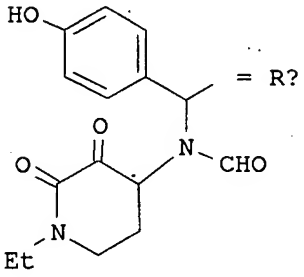


II







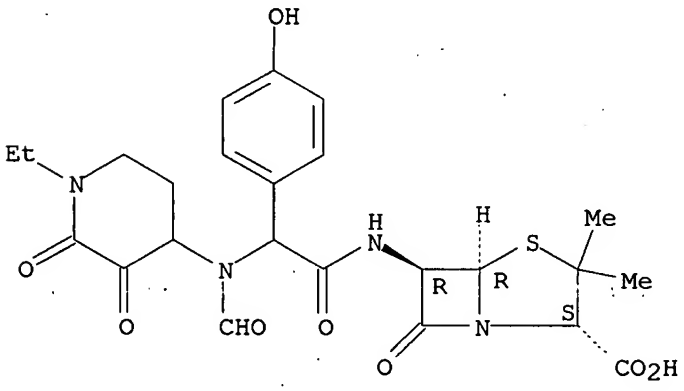
AB The present invention discloses preparation of 6(7)-β-substituted β-lactam compds., such as I and II (R1 = Ra, Rb, Rc; R2 = Me, CMe2CO2H) for their use as inhibitors of β-lactamase activity. Thus, reaction between (Z)-(2-aminothiazol-4-yl)-methoxyiminoacetic acid and tosylate salt of allyl penicillanate afforded ATMO-penicillin allyl ester which upon deacylation afforded ATMO-penicillin II [R1 = Ra (III)]. III exhibited activity against β-lactamases [MIC = 1μg/mL vs. E.coli expressing AmpC β-lactamase; MIC = 1μg/mL vs. E.coli non-expressing AmpC β-lactamase].

IT 637338-86-4P 637338-87-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of sterically-awkward β-lactam derivs. as β-lactamase inhibitors)

RN 637338-86-4 ZCAPLUS

CN 4-Thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid, 6-[[[(1-ethyl-2,3-dioxo-4-piperidinyl)formylamino](4-hydroxyphenyl)acetyl]amino]-3,3-dimethyl-7-oxo-, (2S,5R,6R)- (9CI) (CA INDEX NAME)

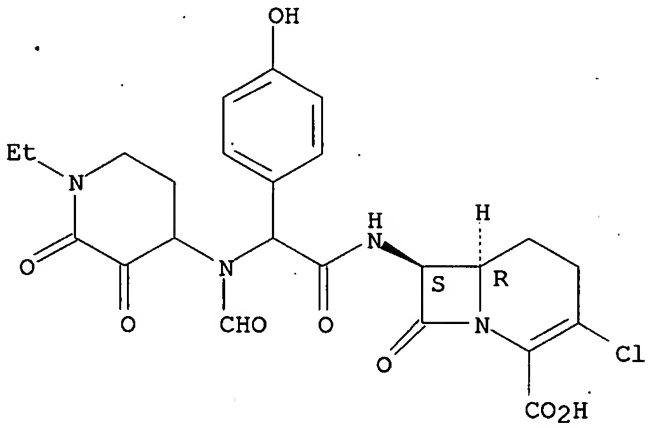
Absolute stereochemistry.



RN 637338-87-5 ZCAPLUS

CN 1-Azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 3-chloro-7-[[[(1-ethyl-2,3-dioxo-4-piperidinyl)formylamino](4-hydroxyphenyl)acetyl]amino]-8-oxo-, (6R,7S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 29 OF 76 ZCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:931324 ZCAPLUS

DOCUMENT NUMBER: 139:381758

TITLE: Preparation of 4-amino-3,7-azepinedione amino acid derivatives as protease inhibitors

INVENTOR(S): Jeong, Jae U.; Yamashita, Dennis S.

PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA

SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

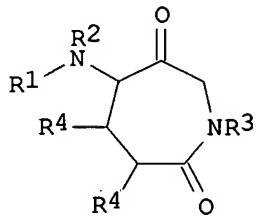
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2003097593	A2	20031127	WO 2003-US16254	20030521
WO 2003097593	A3	20040708		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003263738	A1	20031202	AU 2003-263738	20030521
EP 1511745	A2	20050309	EP 2003-753118	20030521
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2005256100	A1	20051117	US 2004-514965	20041118
PRIORITY APPLN. INFO.:			US 2002-382514P	P 20020522
			WO 2003-US16254	W 20030521

OTHER SOURCE(S): MARPAT 139:381758

GI



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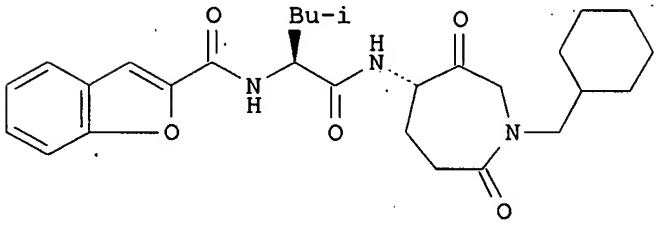


II

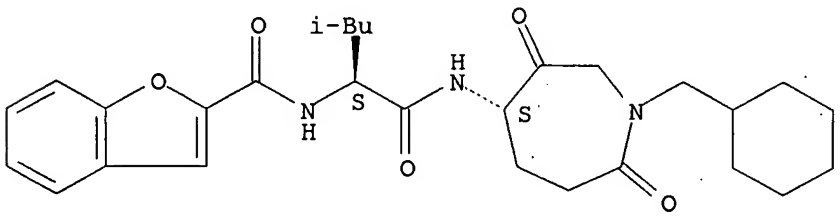
AB The invention relates to 3,7-dioxoazepan-4-ylamides I [R1 is substituted aminoacetyl or 1-amino-C3-7-cycloalkanecarbonyl; R2 is H, alkyl, arylalkyl, heteroarylalkyl; R3 is H, alkyl, cycloalkylalkyl, (hetero)arylalkyl, (thio)acyl, alkylsulfonyl, carbalkoxy, etc.; R4 is H, alkyl, alkoxy, alkylthio, dialkylamino, arylalkyl, etc.] which are protease inhibitors. Thus, compound II was prepared via coupling of 5-amino-N-(cyclohexylmethyl)-6-hydroxy-2-azepinone (preparation given) with N-(tert-butoxycarbonyl)-L-leucine.

IT 624728-11-6P 624728-12-7P 624728-13-8P
624728-14-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of aminoazepinedione amino acid derivs. as protease inhibitors)

RN 624728-11-6 ZCAPLUS

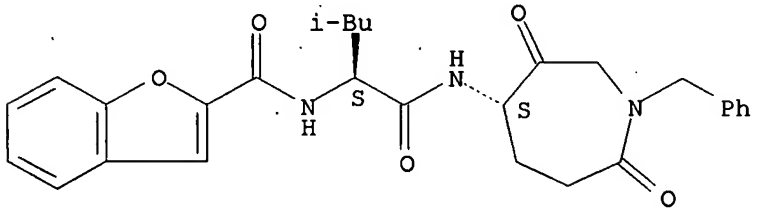
CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[(4S)-1-(cyclohexylmethyl)hexahydro-3,7-dioxo-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



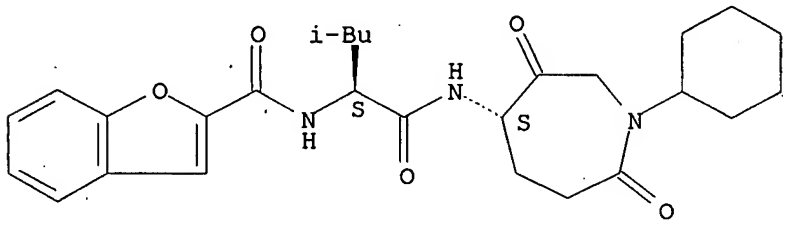
RN 624728-12-7 ZCAPLUS
CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[(4S)-hexahydro-3,7-dioxo-1-(phenylmethyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



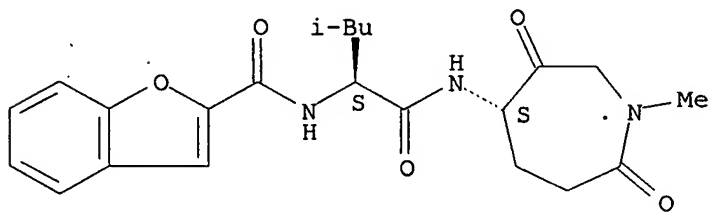
RN 624728-13-8 ZCAPLUS
CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[(4S)-1-cyclohexylhexahydro-3,7-dioxo-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



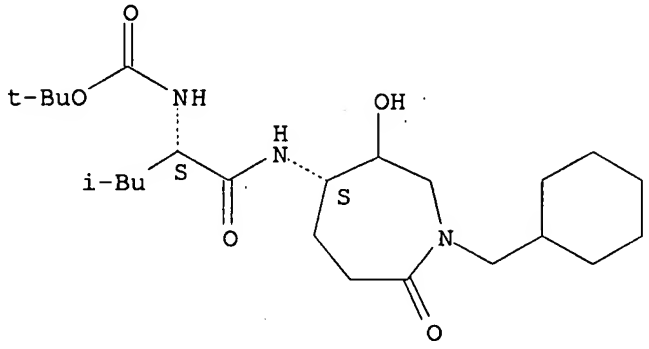
RN 624728-14-9 ZCAPLUS
CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[(4S)-hexahydro-1-methyl-3,7-dioxo-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



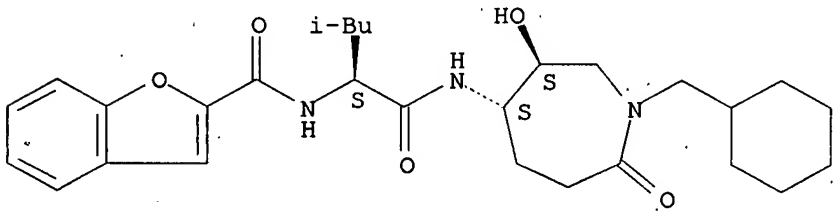
IT 624728-09-2P 624728-10-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of aminoazepinedione amino acid derivs. as protease inhibitors)
RN 624728-09-2 ZCAPLUS
CN Carbamic acid, [(1S)-1-[[[(4S)-1-(cyclohexylmethyl)hexahydro-3-hydroxy-7-oxo-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



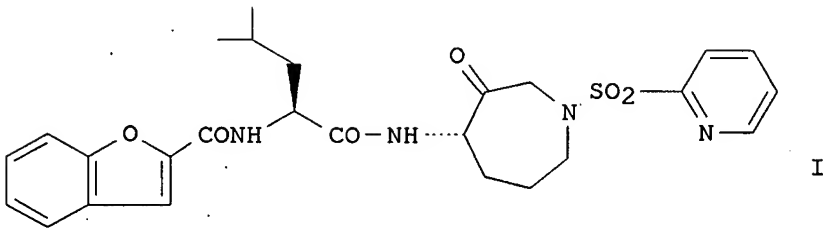
RN 624728-10-5 ZCAPLUS
CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[(3S,4S)-1-(cyclohexylmethyl)hexahydro-3-hydroxy-7-oxo-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 30 OF 76 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:921964 ZCAPLUS
DOCUMENT NUMBER: 140:280693
TITLE: An Azepanone-Based Inhibitor of Human Cathepsin K with Improved Oral Bioavailability in the Rat and the Monkey
AUTHOR(S): Marquis, Robert W.; Ward, Keith W.; Roethke, Theresa; Smith, Brian R.; Ru, Yu; Yamashita, Dennis S.; Tomaszek, Thaddeus A.; Gorycki, Peter D.; Cheng, H.-Y.; James, Ian E.; Stroup, George B.; Lark, Michael W.; Gowen, Maxine; Veber, Daniel F.
CORPORATE SOURCE: Departments of Medicinal Chemistry, Drug Metabolism and Pharmacokinetics, Mechanistic Enzymology Computational Analytical and Structural Sciences and Bone and Cartilage Biology, GlaxoSmithKline, Collegeville, PA, 19426, USA
SOURCE: Molecular Pharmaceutics (2004), 1(1), 97-100
CODEN: MPOHBP; ISSN: 1543-8384

PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



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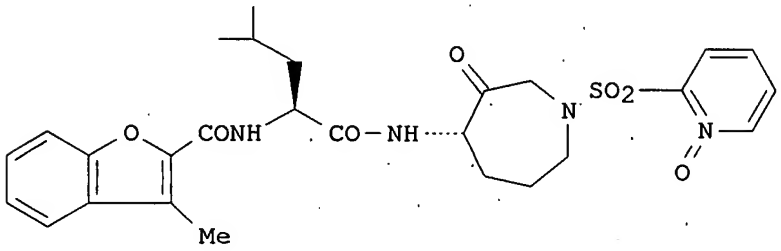


II

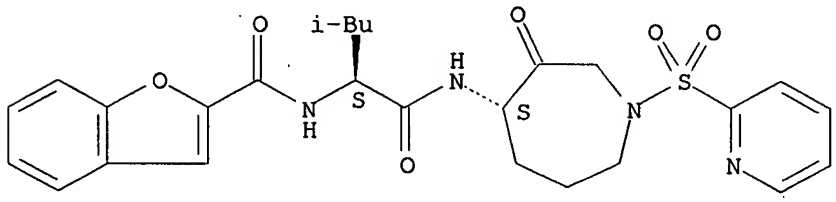
AB Pharmacokinetic evaluation of the potent azepanone-based cathepsin K inhibitor 3 (I) showed that it has an oral bioavailability of 42% in the rat and 4.8% in the monkey. The less than optimal oral bioavailabilities of 3 in the rat and the monkey precluded this analog from being subjected to more detailed pharmacokinetic and pharmacodynamic analyses. In vitro and in vivo studies aimed at identifying the mechanisms which may be limiting the bioavailability of 3 in these species served to guide the syntheses of subsequent analogs for further evaluation. These studies have led to the identification of azepanone 6 (II) that possesses improved oral bioavailability in both the rat (66.3%) and the monkey (23.4%).

IT 281217-45-6 281217-59-2 281217-76-3
281217-83-2
RL: PKT (Pharmacokinetics); PRP (Properties); BIOL (Biological study)
(azepanone-based inhibitor of human cathepsin K with improved oral bioavailability in rat and the monkey)

RN 281217-45-6 ZCAPLUS

CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[(4S)-hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

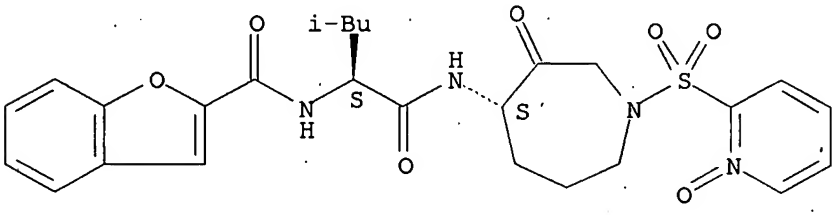
Absolute stereochemistry.



RN 281217-59-2 ZCAPLUS

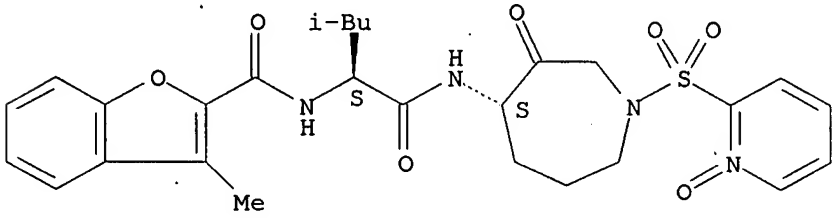
CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[(4S)-hexahydro-1-[(1-oxido-2-pyridinyl)sulfonyl]-3-oxo-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



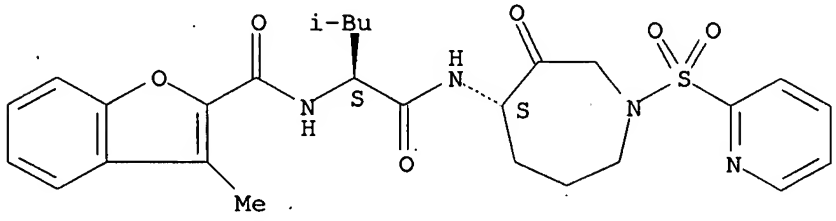
RN 281217-76-3 ZCAPLUS
CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[(4S)-hexahydro-1-[(1-oxido-2-pyridinyl)sulfonyl]-3-oxo-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]-3-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 281217-83-2 ZCAPLUS
CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[(4S)-hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]-3-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

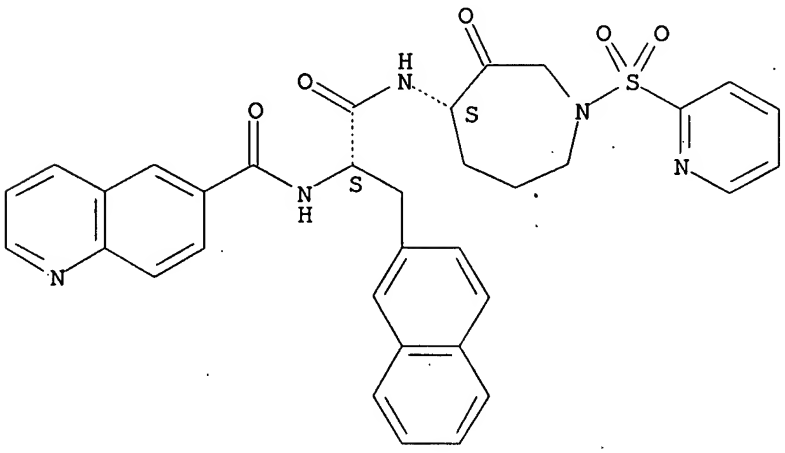


REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 31 OF 76 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:665404 ZCAPLUS
DOCUMENT NUMBER: 141:103796
TITLE: Potent and selective cathepsin L inhibitors do not inhibit human osteoclast resorption in vitro. [Erratum to document cited in CA135:120165]
AUTHOR(S): James, Ian E.; Marquis, Robert W.; Blake, Simon M.; Hwang, Shing Mei; Gress, Catherine J.; Ru, Yu; Zembryki, Denise; Yamashita, Dennis S.; McQueney,

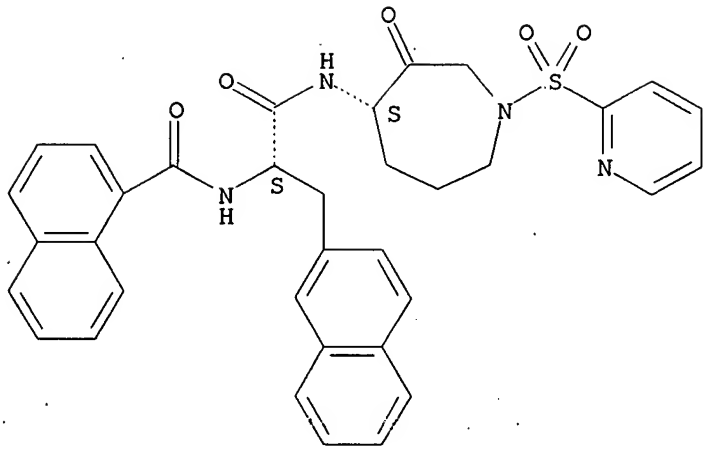
Michael S.; Tomaszek, Thaddeus A.; Oh, Hye-Ja; Gowen, Maxine; Veber, Daniel F.; Lark, Michael W.
CORPORATE SOURCE: Departments of Bone and Cartilage Biology, SmithKline Beecham Pharmaceuticals, King of Prussia, PA, 19406, USA
SOURCE: Journal of Biological Chemistry (2003), 278(34), 32484
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In Tables I and II, analogs SB-468430 and SB-468433 were originally reported to contain the quinoline-8-carboxamide moiety. Subsequent resynthesis revealed that in actuality these analogs contain the isomeric quinoline-6-carboxamide moiety. The modified structures are given in revised Tables I and II. Corrected Ki values for cathepsin L and cathepsin K in Table I are also given.
IT 350796-38-2, SB 468430 350796-39-3 350796-41-7
, SB 468433
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(potent and selective cathepsin L inhibitors do not inhibit human osteoclast resorption in vitro (Erratum))
RN 350796-38-2 ZCAPLUS
CN 6-Quinolinecarboxamide, N-[(1S)-2-[[(4S)-hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]-1-(2-naphthalenylmethyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



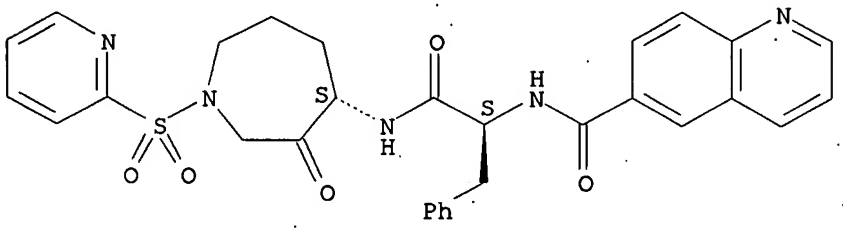
RN 350796-39-3 ZCAPLUS
CN 2-Naphthalenepropanamide, N-[(4S)-hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-α-[(1-naphthalenylcarbonyl)amino]-, (αS)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 350796-41-7 ZCAPLUS
CN 6-Quinolinecarboxamide, N-[(1S)-2-[[(4S)-hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]-2-oxo-1-(phenylmethyl)ethyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 32 OF 76 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:590812 ZCAPLUS
DOCUMENT NUMBER: 139:133836
TITLE: Preparation of 4-aminoazepan-3-ones as protease inhibitors
INVENTOR(S): Marquis, Robert Wells; Ru, Yu; Veber, Daniel Frank; Cummings, Maxwell David; Thompson, Scott Kevin; Yamashita, Dennis Shinji
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: U.S. Pat. Appl. Publ., 126 pp., Cont.-in-part of U.S. Ser. No. 593,845, abandoned.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

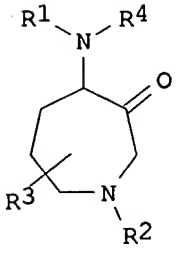
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003144175	A1	20030731	US 2001-881334	20010614
WO 2000038687	A1	20000706	WO 1999-US30730	19991221

W: AE, AL, AU, BA, BB, BG, BR, CA, CN, CZ, EE, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU,

	ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1384713		A1	20040128	EP 2003-76211	19991221
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY				
ZA 2001004208		A	20020523	ZA 2001-4208	20010523
WO 2002017924		A1	20020307	WO 2001-US27178	20010831
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 200186983		A	20020313	AU 2001-86983	20010831
EP 1320370		A1	20030625	EP 2001-966474	20010831
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004509083		T	20040325	JP 2002-522897	20010831
US 2004002487		A1	20040101	US 2003-404716	20030401
US 2005256104		A1	20051117	US 2005-152745	20050614
PRIORITY APPLN. INFO.:				US 1998-113636P	P 19981223
				US 1999-164581P	P 19991110
				WO 1999-US30730	A2 19991221
				US 2000-593845	B2 20000614
				EP 1999-963112	A3 19991221
				US 2000-653815	A2 20000901
				US 2001-881334	A2 20010614
				WO 2001-US27178	W 20010831
				US 2003-404716	B1 20030401

OTHER SOURCE(S): MARPAT 139:133836

GI



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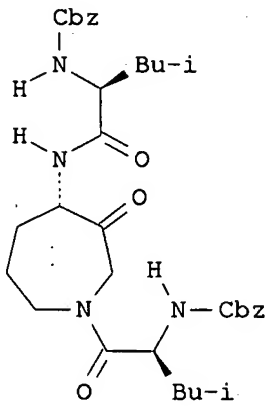


II

AB Aminoazepanones I [R1 = alkanoyl, amino-, alkoxy-, or alkylthioalkanoyl, etc.; R2 = H, alkyl, cycloalkyl, cycloalkylalkyl, (thio)acyl, alkylsulfonyl, etc.; R3 = H, alkyl, cycloalkyl, cycloalkylalkyl, aryl, etc.; R4 = H, alkyl, arylalkyl, etc.] or their pharmaceutically-acceptable

salts were prepared as protease inhibitors, including cathepsin K, for treating diseases of excessive bone loss or cartilage or matrix degradation, gingival disease, arthritis, Paget's disease, hypercalcemia of malignancy, and metabolic bone disease. Thus, compound II (Cbz = benzyloxycarbonyl) was prepared by a multistep procedure.

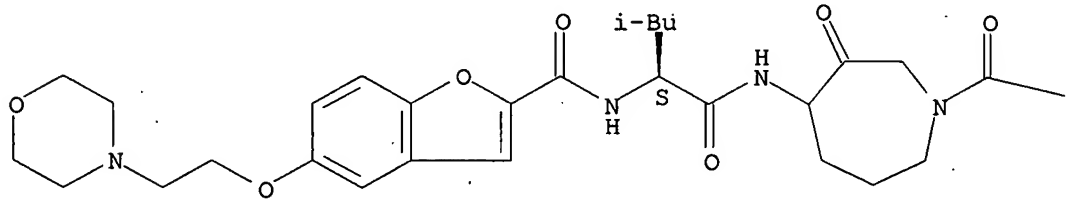
IT 281214-81-1P 281214-85-5P 281214-88-8P
281214-92-4P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of (acylamino)azepanones as protease inhibitors)

RN 281214-81-1 ZCAPLUS

CN 1H-Azepine-1-carboxylic acid, hexahydro-4-[[(2S)-4-methyl-2-[[[5-[2-(4-morpholinyl)ethoxy]-2-benzofuranyl]carbonyl]amino]-1-oxopentyl]amino]-3-oxo-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



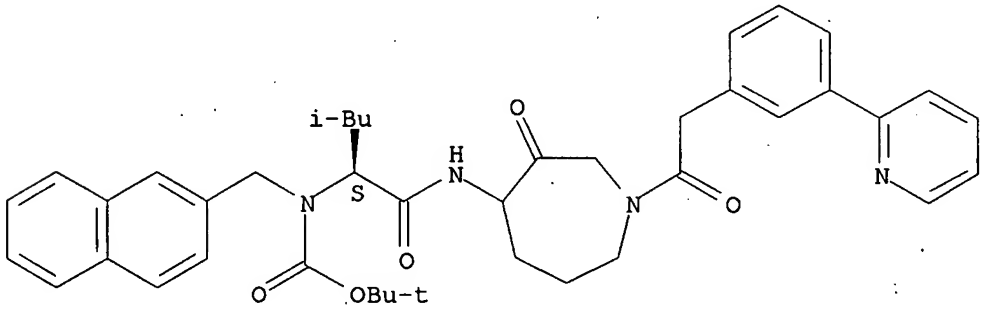
PAGE 1-B

OBu-t

RN 281214-85-5 ZCAPLUS

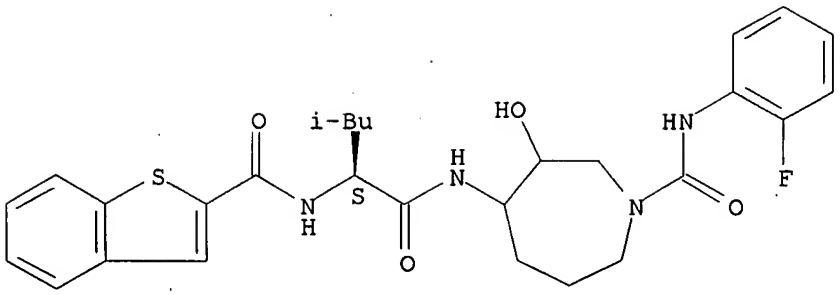
CN Carbamic acid, [(1S)-1-[[[hexahydro-3-oxo-1-[[3-(2-pyridinyl)phenyl]acetyl]-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl](2-naphthalenylmethyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 281214-88-8 ZCAPLUS

CN 1-Piperazinecarboxylic acid, 4-[2-[[2-[[[(1S)-1-[[[hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3-



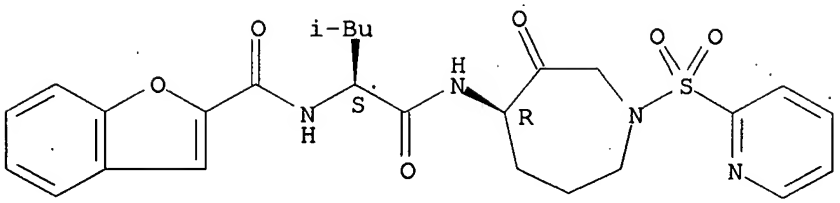
L4 ANSWER 33 OF 76 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:509414 ZCAPLUS
DOCUMENT NUMBER: 140:52478
TITLE: The role of conformational constraint in improved oral bioavailability of cathepsin K inhibitors
AUTHOR(S): Veber, Daniel F.; Marquis, Robert W.; Yamashita, Dennis S.; Ru, Yu; Oh, Hye-Ja; Ward, Keith W.; Smith, Brian R.
CORPORATE SOURCE: SmithKline Beecham Pharmaceuticals, King of Prussia, PA, 19406, USA
SOURCE: Peptides 2000, Proceedings of the European Peptide Symposium, 26th, Montpellier, France, Sept. 10-15, 2000 (2001), Meeting Date 2000, 113-114. Editor(s): Martinez, Jean; Fehrentz, Jean-Alain. Editions EDK: Paris, Fr.
CODEN: 69EDWK; ISBN: 2-84254-048-4
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English

AB A review. We have been engaged in efforts to discover inhibitors of the osteoclast derived cysteine protease, cathepsin K, for use as a bone anti-resorptive to suppress the bone loss characteristic of diseases such as osteoporosis and rheumatoid arthritis. Potent and reversible inhibitors of cathepsin K have been designed but their development as drugs has been limited by poor oral bioavailability and rapid clearance from circulation. This article identifies some cyclic 5 and 6 member ring structures discovered in the course of trying to improve oral bioavailability of ketone-based cathepsin K inhibitors.

IT 281214-75-3 281217-45-6 637345-92-7
637345-94-9
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(role of conformational constraint in improved oral bioavailability of cathepsin K inhibitors)

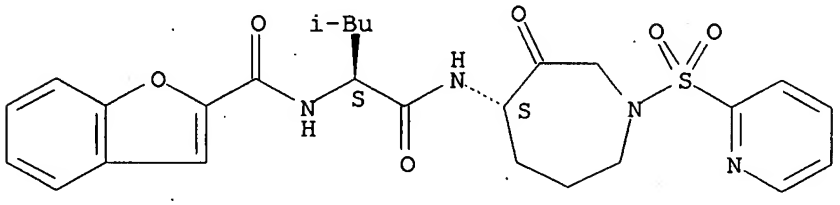
RN 281214-75-3 ZCAPLUS
CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[(4R)-hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



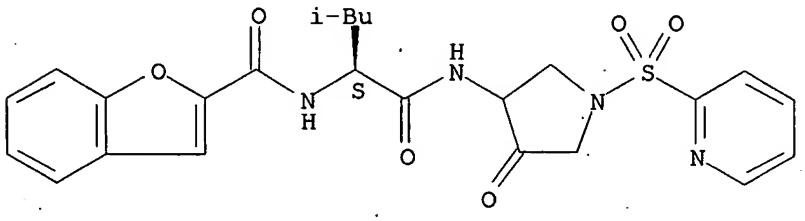
RN 281217-45-6 ZCAPLUS
CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[(4S)-hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



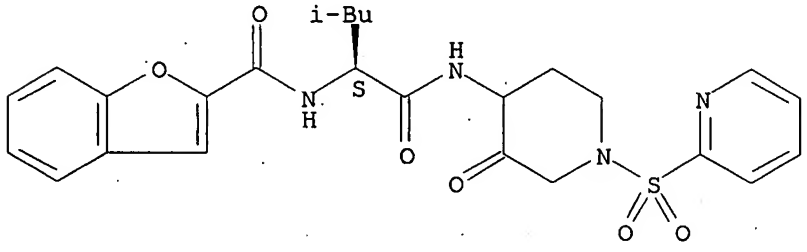
RN 637345-92-7 ZCAPLUS
CN 2-Benzofurancarboxamide, N-[(1S)-3-methyl-1-[[[4-oxo-1-(2-pyridinylsulfonyl)-3-pyrrolidinyl]amino]carbonyl]butyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 637345-94-9 ZCAPLUS
CN 2-Benzofurancarboxamide, N-[(1S)-3-methyl-1-[[[3-oxo-1-(2-pyridinylsulfonyl)-4-piperidinyl]amino]carbonyl]butyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 34 OF 76 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:434525 ZCAPLUS
DOCUMENT NUMBER: 139:22118
TITLE: Methods and intermediates for the synthesis of azepines
INVENTOR(S): Conde, Jose J.
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 70 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

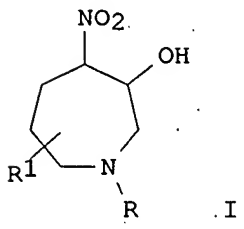
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003045909	A2	20030605	WO 2002-US37423	20021120
WO 2003045909	A3	20031211		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2002360409	A1	20030610	AU 2002-360409	20021120
PRIORITY APPLN. INFO.:			US 2001-331949P	P 20011121
			WO 2002-US37423	W 20021120

OTHER SOURCE(S): CASREACT 139:22118; MARPAT 139:22118
GI



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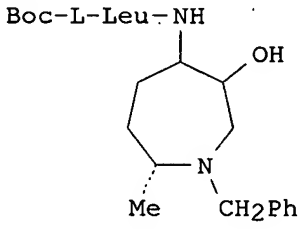


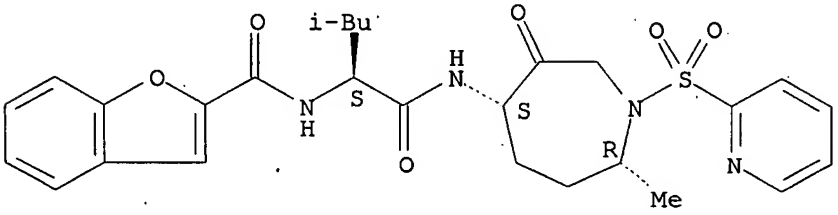
II

AB Azepines I [R alkyl, aryl, acyl, thioacyl; R1 = alkyl] were prepared by cyclizing O2NCH2CHR2CHR3CHR4NRCH2CHO [at least two of R2-R4 = H, the other = alkyl]. Thus, CH2:CHCOMe was treated with MeNO2 to give O2N(CH2)3COMe which was treated with PhCH2NHCH2CO2Et and resolved to give (R)-O2N(CH2)3CHMeN(CH2Ph)CH2CO2Et. This ester was reduced to (R)-O2N(CH2)3CHMeN(CH2Ph)CH2CHO and cyclized over Amberlyst A-21 to give the azepine II [R5 = NO2]. The NO2 group was reduced and acylated with Boc-Leu-OH to give II [R5 = Boc-Leu-NH].

IT 362505-84-8P
RL: PNU (Preparation, unclassified); PREP (Preparation)
(methods and intermediates for synthesis of azepines)

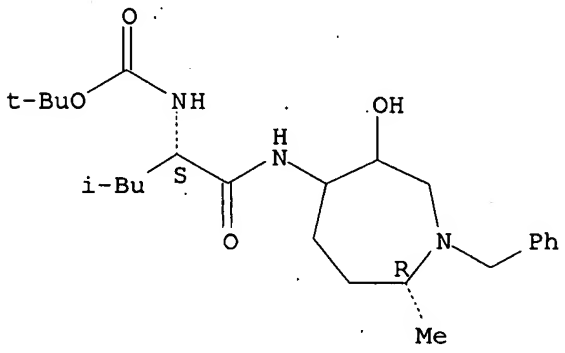
RN 362505-84-8 ZCAPLUS
CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[(4S,7R)-hexahydro-7-methyl-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (CA INDEX NAME)

Absolute stereochemistry.



IT 537033-20-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(methods and intermediates for synthesis of azepines)
RN 537033-20-8 ZCAPLUS
CN Carbamic acid, [(1S)-1-[[[(7R)-hexahydro-3-hydroxy-7-methyl-1-(phenylmethyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 35 OF 76 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:242294 ZCAPLUS
DOCUMENT NUMBER: 138:271977
TITLE: Novel compounds and compositions as Cathepsin inhibitors
INVENTOR(S): Graupe, Michael; Palmer, James T.; Aldous, David J.; Thurairatnam, Sukanthini
PATENT ASSIGNEE(S): Aventis Pharmaceuticals Inc., USA; Celera
SOURCE: PCT Int. Appl., 101 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003024924	A1	20030327	WO 2002-US29323	20020916

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,

GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF,
CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2460125	A1	20030327	CA 2002-2460125	20020916
AU 2002333657	A1	20030401	AU 2002-333657	20020916
EP 1436255	A1	20040714	EP 2002-798975	20020916
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BR 2002012535	A	20041019	BR 2002-12535	20020916
CN 1553892	A	20041208	CN 2002-817890	20020916
JP 2005504078	T	20050210	JP 2003-528772	20020916
NZ 531352	A	20060127	NZ 2002-531352	20020916
US 2004192742	A1	20040930	US 2004-787367	20040226
US 7196099	B2	20070327		
ZA 2004001882	A	20050418	ZA 2004-1882	20040308
NO 2004000996	A	20040512	NO 2004-996	20040309
IN 2004CN00549	A	20051223	IN 2004-CN549	20040312
US 2007135386	A1	20070614	US 2007-625369	20070122
PRIORITY APPLN. INFO.:			US 2001-322318P	P 20010914
			WO 2002-US29323	W 20020916
			US 2004-787367	A3 20040226

OTHER SOURCE(S): MARPAT 138:271977.

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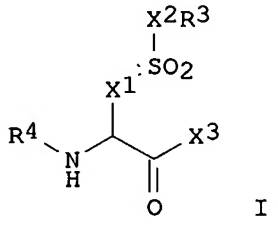

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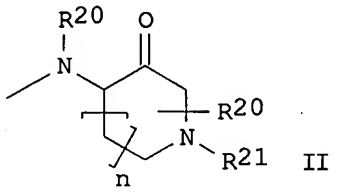

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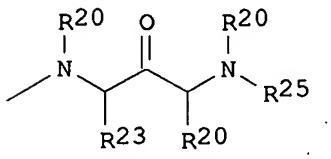
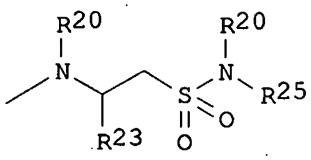


III



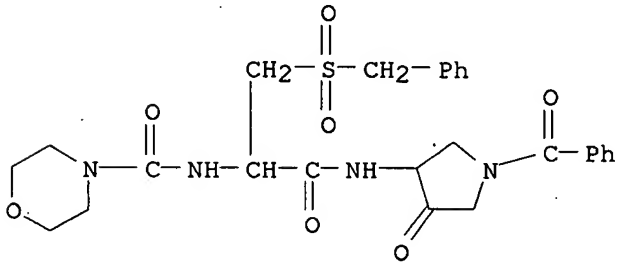
IV

AB Compds. I [X1 = X2 methylene, or X1 = ethylene and X2 is a bond; R3 = CR5:CHR6, CR5(CR63)2, CR7:NR8 [R5 = H and R6 = H, or alkyl, or R5, R6 together and R7, R8 together form (hetero)cycloalkenyl, (hetero)aryl, (hetero)bicycloaryl], (un)substituted alkyl, cyano, halo, nitro, etc.; R4 = (un)substituted COX5R11, SO2X5R11 [X5 is a bond, O, NH, or aminoalkyl; R11 = (un)substituted alkyl]; X3 is group II, III, or IV [n = 0-2; R20 = H, alkyl, (hetero)cycloalkylalkyl, (hetero)arylalkyl; R21 = H, alkyl, (hetero)cycloalkylalkyl, (hetero)arylalkyl, (hetero)bicycloalkyl, (hetero)bicycloarylalkyl, etc.; R23 and R25 = (un)substituted (hetero)alkyl, alkenyl, (hetero)cycloalkylalkyl, etc.]] were prepared as cathepsin S inhibitors. Thus, 2-amino-2-methyl-1-(2-phenyl-[1,3]dithian-2-yl)-propan-1-ol prepared by addition of (1,1-dimethyl-2-oxo-ethyl)-carbamic

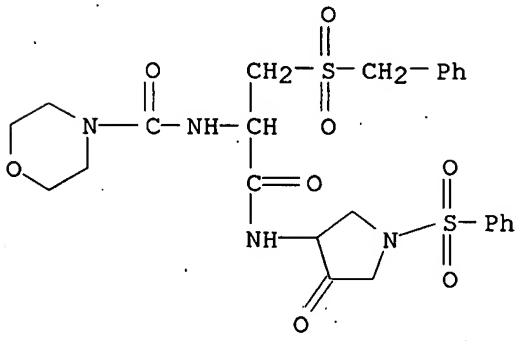
acid tert-Bu ester to 2-phenyl-1,3-dithiane and deprotection was coupled with 2-[(morpholine-4-carbonyl)-amino]-3-phenylmethanesulfonyl-propionic acid, and after treatment with calcium carbonate and mercury chloride, followed by Dess-Martin oxidation gave morpholine-4-carboxylic acid [1-(2-hydroxy-1,1-dimethyl-3-oxo-3-phenylpropylcarbamoyl)-2-phenylmethanesulfonylethyl]amide. The inhibition consts. for compds. of the invention against Cathepsin S were in the range from about 10-10 M to about 10-7 M.

IT 503323-64-6P 503323-65-7P 503323-66-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of cathepsin S inhibitors by peptide coupling and oxidn)

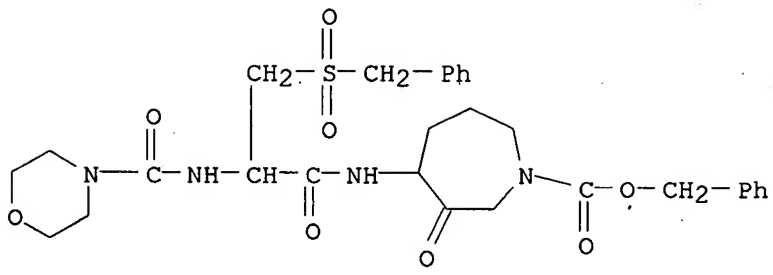
RN 503323-64-6 ZCAPLUS
CN 4-Morpholinecarboxamide, N-[2-[(1-benzoyl-4-oxo-3-pyrrolidinyl)amino]-2-oxo-1-[[(phenylmethyl)sulfonyl]methyl]ethyl]- (9CI) (CA INDEX NAME)



RN 503323-65-7 ZCAPLUS
CN 4-Morpholinecarboxamide, N-[2-oxo-2-[[4-oxo-1-(phenylsulfonyl)-3-pyrrolidinyl]amino]-1-[[(phenylmethyl)sulfonyl]methyl]ethyl]- (9CI) (CA INDEX NAME)

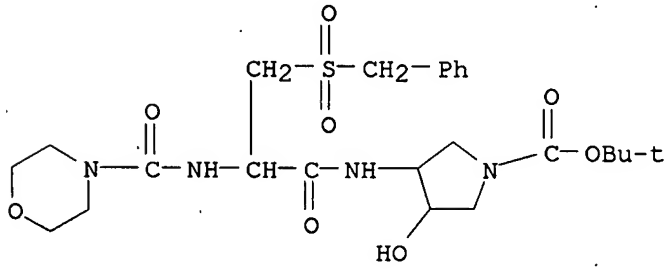


RN 503323-66-8 ZCAPLUS
CN 1H-Azepine-1-carboxylic acid, hexahydro-4-[[2-[(4-morpholinylcarbonyl)amino]-1-oxo-3-[(phenylmethyl)sulfonyl]propyl]amino]-3-oxo-, phenylmethyl ester (9CI) (CA INDEX NAME)



IT 503323-82-8P 503323-84-0P 503323-85-1P
503323-86-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of cathepsin S inhibitors by peptide coupling and oxidn)

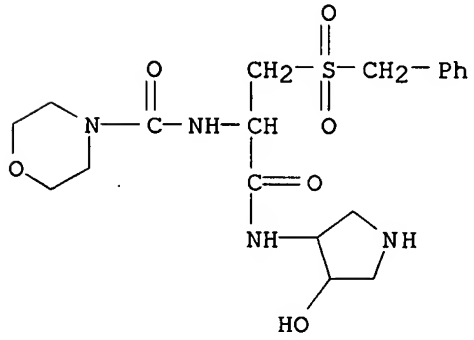
RN 503323-82-8 ZCAPLUS
CN 1-Pyrrolidinecarboxylic acid, 3-hydroxy-4-[[2-[(4-morpholinylcarbonyl)amino]-1-oxo-3-[(phenylmethyl)sulfonyl]propyl]amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 503323-84-0 ZCAPLUS
CN 4-Morpholinecarboxamide, N-[2-[(4-hydroxy-3-pyrrolidinyl)amino]-2-oxo-1-[[(phenylmethyl)sulfonyl]methyl]ethyl]-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

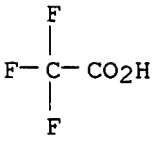
CM 1

CRN 503323-83-9
CMF C19 H28 N4 O6 S

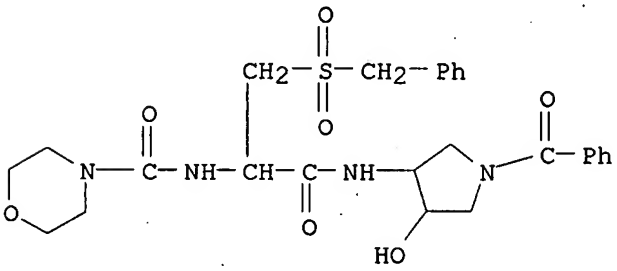


CM 2

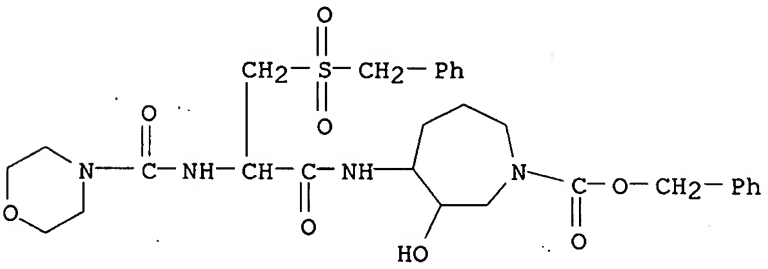
CRN 76-05-1
CMF C2 H F3 O2



RN 503323-85-1 ZCAPLUS
CN 4-Morpholinecarboxamide, N-[2-[(1-benzoyl-4-hydroxy-3-pyrrolidinyl)amino]-2-oxo-1-[[(phenylmethyl)sulfonyl]methyl]ethyl]- (9CI) (CA INDEX NAME)



RN 503323-86-2 ZCAPLUS
CN 1H-Azepine-1-carboxylic acid, hexahydro-3-hydroxy-4-[[2-[(4-morpholinylcarbonyl)amino]-1-oxo-3-[(phenylmethyl)sulfonyl]propyl]amino]-, phenylmethyl ester (9CI) (CA INDEX NAME)



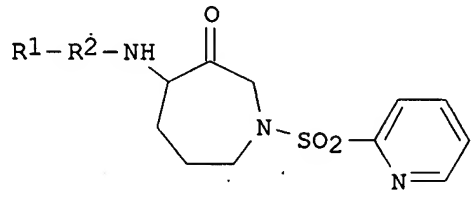
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 36 OF 76 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:888706 ZCAPLUS
DOCUMENT NUMBER: 137:370363
TITLE: Preparation of 4-amino-azepan-3-one derivatives as protease inhibitors
INVENTOR(S): Xie, Ren; Yamashita, Dennis S.
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2002092563	A2	20021121	WO 2002-US15376		20020515
WO 2002092563	A3	20030403			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
AU 2002342682	A1	20021125	AU 2002-342682		20020515
EP 1401453	A2	20040331	EP 2002-744152		20020515
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
JP 2004527575	T	20040909	JP 2002-589449		20020515
US 2004157828	A1	20040812	US 2003-478619		20031117
PRIORITY APPLN. INFO.:			US 2001-291545P	P	20010517
			US 2001-292646P	P	20010522
			WO 2002-US15376	W	20020515

OTHER SOURCE(S): MARPAT 137:370363

GI



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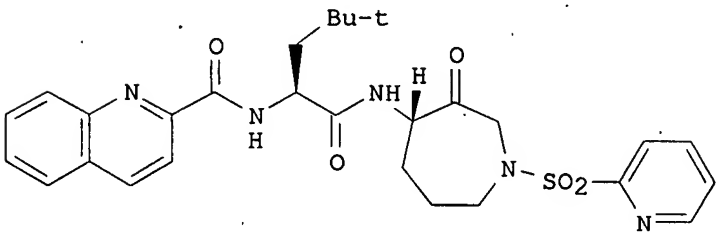


II

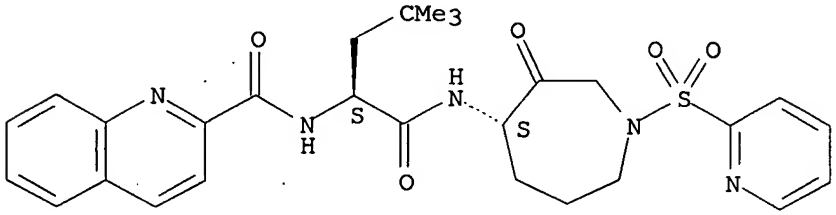
AB 4-Aminoazepan-3-one derivs. of formula I [R1 = 3-methylbenzofuran-2-carbonyl, benzofuran-2-carbonyl, 5-methoxybenzofuran-2-carbonyl, benzothiophene-2-carbonyl, quinoline-2-carbonyl, quinoline-3-carbonyl, thiophene-2-carbonyl, thiophene-3-carbonyl, 5-methylthiophene-2-carbonyl, furan-2-carbonyl, furan-3-carbonyl, thieno[3,2-b]thiophene-2-carbonyl; R2 = L-tert-butylalaninyl, L-2-thiophenylalaninyl, L-cyclohexylglycinyl, L-allo-isoleucinyl, tetrahydroisoquinoline-3-carbonyl, L-prolinyl, (S)-2-amino-4-methanesulfonylbutanoyl, (S)-piperidine-2-carbonyl] are prepared which inhibit proteases, including cathepsin K. The compds. are useful for treating diseases of excessive bone loss or cartilage or matrix degradation, including osteoporosis, gingival disease including gingivitis and periodontitis, arthritis, more specifically, osteoarthritis and rheumatoid arthritis, Paget's disease, hypercalcemia of malignancy, and metabolic

bone disease. Thus, II was prepared from 4-amino-3-hydroxyazepane-1-carboxylic acid benzyl ester hydrochloride, 2-pyridinesulfonyl chloride, Boc-L-tert-butylalanine and quinaldic acid. The prepared compds. had Ki values between 2 nM and 1000 nM against cathepsin K in inhibition assays.

IT 475285-72-4P 475285-73-5P 475285-74-6P
475285-75-7P 475285-76-8P 475285-77-9P
475285-78-0P 475285-79-1P 475285-80-4P
475285-81-5P 475285-82-6P 475285-83-7P
475285-84-8P 475285-85-9P 475285-86-0P
475285-87-1P 475285-88-2P 475285-89-3P
475285-90-6P 475285-91-7P 475285-92-8P
475285-93-9P 475285-94-0P 475285-95-1P
475285-96-2P 475285-97-3P 475285-98-4P
475285-99-5P 475286-00-1P 475286-01-2P
475286-02-3P 475286-03-4P 475286-04-5P
475286-05-6P 475286-06-7P 475286-07-8P
475286-08-9P 475286-09-0P 475286-10-3P
475286-11-4P 475286-12-5P 475286-13-6P
475286-14-7P 475286-15-8P 475286-16-9P
475286-17-0P 475286-18-1P 475286-19-2P
475286-44-3P 475286-45-4P 475286-46-5P
475286-47-6P 475286-48-7P 475286-49-8P
475286-50-1P 475286-51-2P 475286-52-3P
475286-53-4P 475286-54-5P 475286-55-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of aminoazepanone derivs. as protease inhibitors)

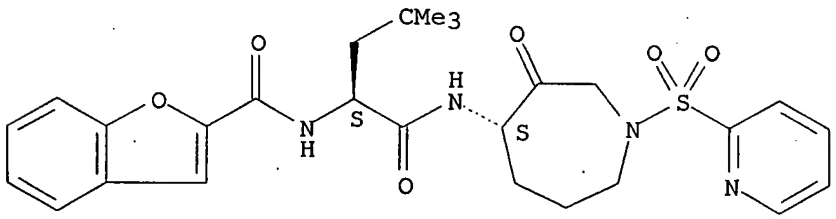
RN 475285-72-4 ZCAPLUS
CN 2-Quinolinecarboxamide, N-[(1S)-1-[[[(4S)-hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3,3-dimethylbutyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



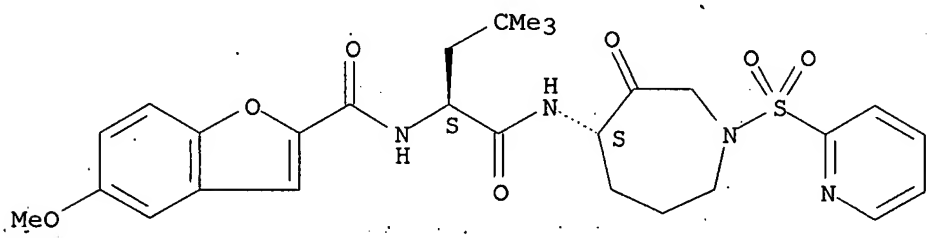
RN 475285-73-5 ZCAPLUS
CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[(4S)-hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3,3-dimethylbutyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



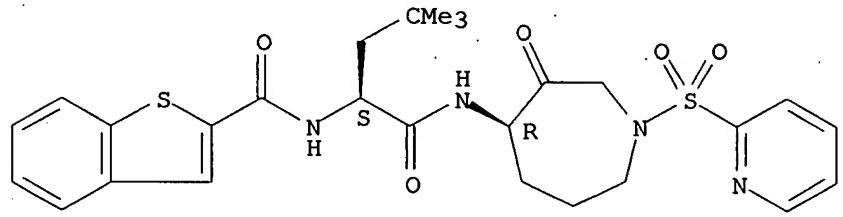
RN 475285-74-6 ZCAPLUS
CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[(4S)-hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3,3-dimethylbutyl]-5-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



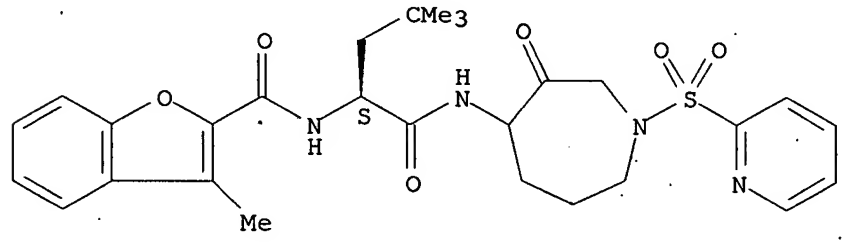
RN 475285-75-7 ZCAPLUS
CN Benzo[b]thiophene-2-carboxamide, N-[(1S)-1-[[[(4R)-hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3,3-dimethylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 475285-76-8 ZCAPLUS
CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3,3-dimethylbutyl]-3-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 475285-77-9 ZCAPLUS
CN 3-Quinolinecarboxamide, N-[(1S)-1-[[[hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3,3-dimethylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

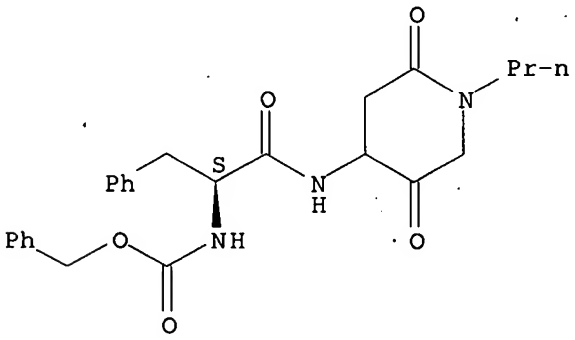
L4 ANSWER 37 OF 76 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:732400 ZCAPLUS
DOCUMENT NUMBER: 138:331183
TITLE: General solid-phase method to prepare novel cyclic ketone inhibitors of the cysteine protease cruzain
AUTHOR(S): Huang, Lily; Ellman, Jonathan A.
CORPORATE SOURCE: Department of Chemistry, Center for New Directions in Organic Synthesis, University of California, Berkeley, CA, 94720, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2002), 12(20), 2993-2996
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 138:331183

AB A series of constrained ketone-based inhibitors has been developed that show low nanomolar Ki values. These ketone inhibitors showed promising activity towards cruzain, the cysteine protease implicated in Chagas' disease. This series of constrained inhibitors, which can be accessed quickly and efficiently using a solid-phase combinatorial strategy, should be applicable to other members of the cysteine protease class.

IT 515152-30-4P 515152-31-5P 515152-32-6P
515152-33-7P 515152-34-8P 515152-35-9P
515152-36-0P
RL: CPN (Combinatorial preparation); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); CMBI (Combinatorial study); PREP (Preparation); USES (Uses)
(solid-phase preparation of cyclic ketone inhibitors of cruzain)

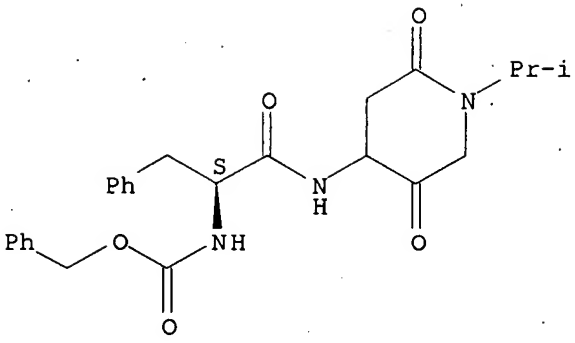
RN 515152-30-4 ZCAPLUS
CN Carbamic acid, [(1S)-2-[(2,5-dioxo-1-propyl-4-piperidinyl)amino]-2-oxo-1-(phenylmethyl)ethyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



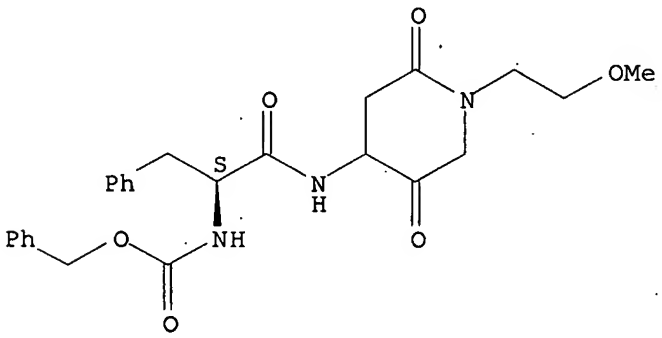
RN 515152-31-5 ZCAPLUS
CN Carbamic acid, [(1S)-2-[[1-(1-methylethyl)-2,5-dioxo-4-piperidinyl]amino]-2-oxo-1-(phenylmethyl)ethyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



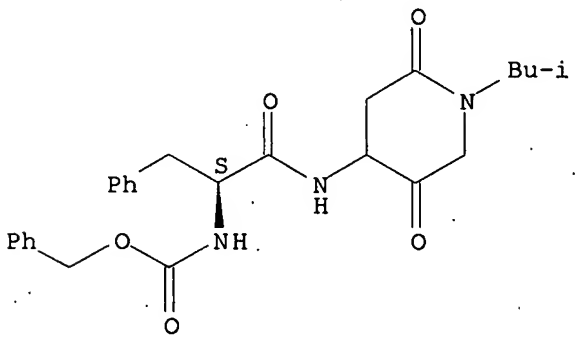
RN 515152-32-6 ZCAPLUS
CN Carbamic acid, [(1S)-2-[[1-(2-methoxyethyl)-2,5-dioxo-4-piperidinyl]amino]-2-oxo-1-(phenylmethyl)ethyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



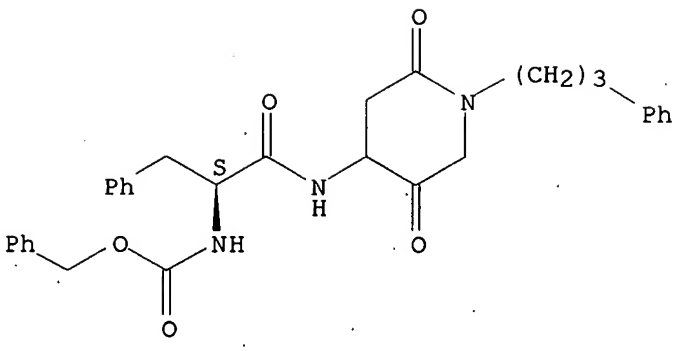
RN 515152-33-7 ZCAPLUS
CN Carbamic acid, [(1S)-2-[[1-(2-methylpropyl)-2,5-dioxo-4-piperidinyl]amino]-2-oxo-1-(phenylmethyl)ethyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



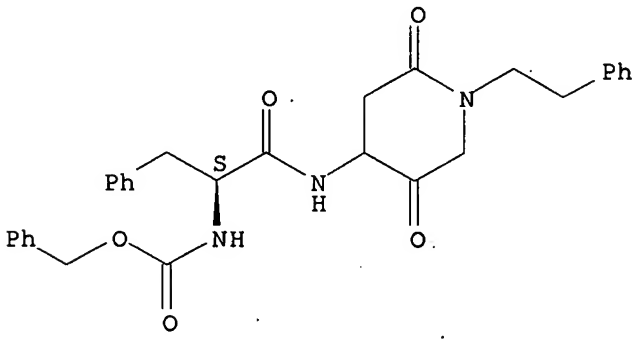
RN 515152-34-8 ZCAPLUS
CN Carbamic acid, [(1S)-2-[[2,5-dioxo-1-(3-phenylpropyl)-4-piperidinyl]amino]-2-oxo-1-(phenylmethyl)ethyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



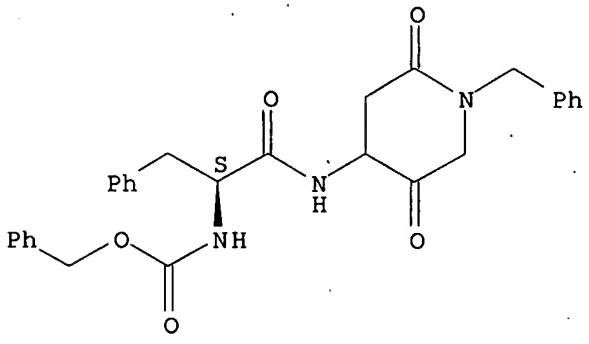
RN 515152-35-9 ZCAPLUS
CN Carbamic acid, [(1S)-2-[[2,5-dioxo-1-(2-phenylethyl)-4-piperidinyl]amino]-2-oxo-1-(phenylmethyl)ethyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 515152-36-0 ZCAPLUS
CN Carbamic acid, [(1S)-2-[[2,5-dioxo-1-(phenylmethyl)-4-piperidinyl]amino]-2-oxo-1-(phenylmethyl)ethyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 38 OF 76 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:339678 ZCAPLUS
DOCUMENT NUMBER: 138:100849
TITLE: A potent small molecule, nonpeptide inhibitor of

cathepsin K (SB 331750) prevents bone matrix resorption in the ovariectomized rat

AUTHOR(S): Lark, M. W.; Stroup, G. B.; James, I. E.; Dodds, R. A.; Hwang, S. M.; Blake, S. M.; Lechowska, B. A.; Hoffman, S. J.; Smith, B. R.; Kapadia, R.; Liang, X.; Erhard, K.; Ru, Y.; Dong, X.; Marquis, R. W.; Veber, D.; Gowen, M.

CORPORATE SOURCE: Department of Bone and Cartilage Biology, SmithKline Beecham Pharmaceuticals, King of Prussia, PA, USA

SOURCE: Bone (New York, NY, United States) (2002), 30(5), 746-753
CODEN: BONEDL; ISSN: 8756-3282

PUBLISHER: Elsevier Science Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Inhibition of the cysteine proteinase, cathepsin K (E.C. 3.4.22.38) has been postulated as a means to control osteoclast-mediated bone resorption. The preferred animal models for evaluation of antiresorptive activity are in the rat. However, the development of compds. that inhibit rat cathepsin K has proven difficult because the human and rat enzymes differ in key residues in the active site. In this study, a potent, nonpeptide inhibitor of rat cathepsin K (Ki = 4.7 nmol/L), 5-(2-morpholin-4-yl-ethoxy)-benzofuran-2-carboxylic acid ((S)-3-methyl-1-{3-oxo-1-[2-(3-pyridin-2-yl-phenyl)-ethenoyl]-azepan-4-ylcarbanoyl}-butyl)-amide (SB 331750), is described, which is efficacious in rat models of bone resorption. SB 331750 potently inhibited human cathepsin K activity in vitro (Ki = 0.0048 nmol/L) and was selective for human cathepsin K vs. cathepsins B (Ki = 100 nmol/L), L (0.48 nmol/L), or S (Ki = 14.3 nmol/L). In an in situ enzyme assay, SB 331750 inhibited osteoclast-associated cathepsin activity in tissue sections containing human osteoclasts (IC50 .apprx. 60 nmol/L) and this translated into potent inhibition of human osteoclast-mediated bone resorption in vitro (IC50 .apprx. 30 nmol/L). In vitro, SB 331750 partially, but dose-dependently, prevented the parathyroid hormone-induced hypercalcemia in an acute rat model of bone resorption. To evaluate the ability of SB 331750 to inhibit bone matrix degradation in vivo, it was administered for 4 wk at 3, 10, or 30 mg/kg, i.p., u.i.d. in the ovariectomized (ovx) rat. Both 10 and 30 mg/kg doses of compound prevented the ovx-induced elevation in urinary deoxypyridinoline and prevented the ovx-induced increase in percent eroded perimeter. Histol. evaluation of the bones from compound-treated animals indicated that SB 331750 retarded bone matrix degradation in vivo at all three doses. The inhibition of bone resorption at the 10 and 30 mg/kg doses resulted in prevention of the ovx-induced reduction in percent trabecular area, trabecular number, and increase in trabecular spacing. These effects on bone resorption were also reflected in inhibition of the ovx-induced loss in trabecular bone volume as assessed using microcomputerized tomog. (μCT; .apprx.60% at 30 mg/kg). Together, these data indicate that the cathepsin K inhibitor, SB 331750, prevented bone resorption in vivo and this inhibition resulted in prevention of ovariectomy-induced loss in trabecular structure.

IT 486442-96-0, SB 331750
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(potent small mol., nonpeptide inhibitor of cathepsin K (SB 331750) prevents bone matrix resorption in ovariectomized rat)

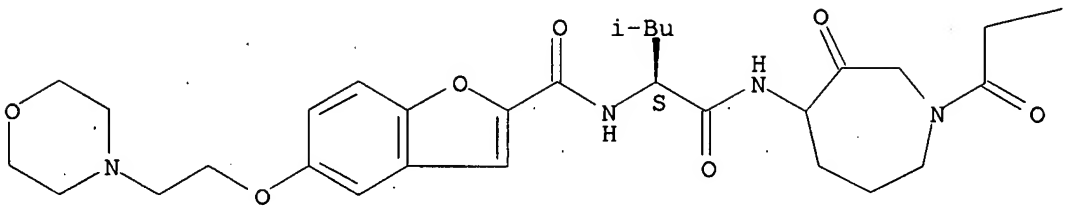
RN 486442-96-0 ZCAPLUS

CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[hexahydro-3-oxo-1-[[3-(2-pyridinyl)phenyl]acetyl]-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]-5-[2-(4-morpholinyl)ethoxy]- (9CI) (CA INDEX NAME)

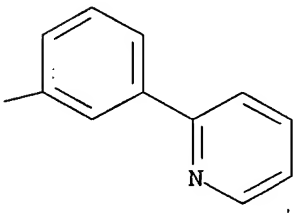
Absolute stereochemistry.

Currently available stereo shown.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

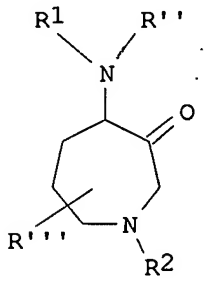
L4 ANSWER 39 OF 76 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:171694 ZCAPLUS
DOCUMENT NUMBER: 136:232208
TITLE: Preparation of 4-aminoazepan-3-one parasitic cysteine protease inhibitors effective against malaria and other diseases
INVENTOR(S): Tew, David G.; Thompson, Scott K.; Veber, Daniel F.
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, UK
SOURCE: PCT Int. Appl., 220 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002017924	A1	20020307	WO 2001-US27178	20010831
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003144175	A1	20030731	US 2001-881334	20010614
AU 200186983	A	20020313	AU 2001-86983	20010831
EP 1320370	A1	20030625	EP 2001-966474	20010831

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

JP 2004509083 T 20040325 JP 2002-522897 20010831
PRIORITY APPLN. INFO.: US 2000-653815 A2 20000901
US 2001-881334 A2 20010614
US 1998-113636P P 19981223
US 1999-164581P P 19991110
WO 1999-US30730 A2 19991221
US 2000-593845 B2 20000614
WO 2001-US27178 W 20010831
OTHER SOURCE(S): MARPAT 136:232208

GI



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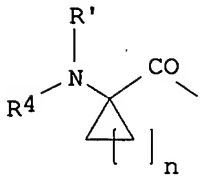


II

AB The present invention relates to methods of treating parasitic diseases which are mediated by cysteine proteases by administration of 4-aminoazepan-3-one protease inhibitors I (e.g. benzo[1,3]dioxole-5-carboxylic acid [(S)-1-(1-benzyl-3-oxoazepan-4-ylcarbamoyl)-3-methylbutyl]amide) and pharmaceutically acceptable salts, hydrates and solvates thereof. In particular, the present invention relates to a method of treating malaria by inhibiting the cysteine protease falcipain. Other diseases against which the claimed compds. are effective include trypanosomiasis (African sleeping sickness, Chagas disease), leishmaniasis, schistosomiasis, onchocerciasis (river blindness) and giardiasis. In I: R1 is R4NR'CHR3C(O)-, R5XCHR3C(O)-, R3CH2C(O)-, R4NR'CR''''R3C(O)-, II. R2 is H, C1-6alkyl, C3-6cycloalkyl-C0-6alkyl, Ar-C0-6alkyl, Het-C0-6alkyl, R9C(O)-, R9C(S)-, R9SO2-, R9OC(O)-, R9R11NC(O)-, R9R11NC(S)-, R9(R11)NSO2-, 3-(2-pyridyl)benzylcarbonyl, 2-(3-(2-pyridyl)phenyl)ethyl, R7NR6CHR8Z-, and R9SO2R11NC(O)-. R3 is H, C1-6alkyl, C3-6cycloalkyl-C0-6alkyl, C2-6alkenyl, C2-6alkynyl, HetC0-6alkyl and ArC0-6alkyl. R3 and R' may be connected to form a pyrrolidine, piperidine or morpholine ring. R4 is H, C1-6alkyl, C3-6cycloalkyl-C0-6alkyl, Ar-C0-6alkyl, Het-C0-6alkyl, R5C(O)-, R5C(S)-, R5SO2-, R5OC(O)-, R5R12NC(O)-, and R5R12NC(S)-. R5 is H, C1-6alkyl, C2-6alkenyl, C2-6alkynyl, C3-6cycloalkyl-C0-6alkyl, Ar-C0-6alkyl and Het-C0-6alkyl. R6 is H, C1-6alkyl, Ar-C0-6alkyl, and Het-C0-6alkyl. R7 is H, C1-6alkyl, C3-6cycloalkyl-C0-6alkyl, Ar-C0-6alkyl, Het-C0-6alkyl, R10C(O)-, R10C(S)-, R10SO2-, R10OC(O)-, R10R13NC(O)-, and R10R13NC(S)-. R8 is H, C1-6alkyl, C2-6alkenyl, C2-6alkynyl, HetC0-6alkyl and ArC0-6alkyl. R9, R10 independently = C1-6alkyl, C3-6cycloalkyl-C0-6alkyl, Ar-C0-6alkyl and Het-C0-6alkyl. R11, R12, R13, R', R'' independently = H, C1-6alkyl, Ar-C0-6alkyl, and Het-C0-6alkyl. R''' is H, C1-6alkyl, C3-6cycloalkyl-C0-6alkyl, Ar-C0-6alkyl, and Het-C0-6alkyl; R'''' is C1-6alkyl, C3-6cycloalkyl-C0-6alkyl C2-6alkenyl, C2-6alkynyl, HetC0-6alkyl and ArC0-6alkyl. X is CH2, S, and O; Z is C(O) and CH2; n is 1-5. Although the methods of preparation are not claimed, 220 example prepns. are included.

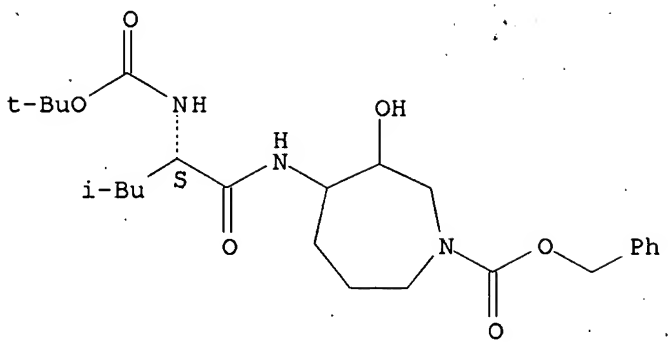
IT 281219-34-9P, 4-[(S)-2-[(tert-Butoxycarbonyl)amino]-4-

methylpentanoylamino]-3-hydroxyazepan-1-carboxylic acid benzyl ester 281219-35-0P, [(1S)-1-[(3-Hydroxyazepan-4-yl)carbamoyl]-3-methylbutyl]carbamic acid tert-butyl ester 281219-36-1P, [(1S)-1-[(1-Benzyl-3-hydroxyazepan-4-yl)carbamoyl]-3-methylbutyl]carbamic acid tert-butyl ester 281219-37-2P, (S)-2-Amino-4-methylpentanoic acid (1-benzyl-3-hydroxyazepan-4-yl)amide 281219-39-4P, Benzo[1,3]dioxole-5-carboxylic acid [(1S)-1-[(1-benzyl-3-hydroxyazepan-4-yl)carbamoyl]-3-methylbutyl]amide 281219-45-2P, [(1S)-3-Methyl-1-[[3-hydroxy-1-[2-(3-(pyridin-2-yl)phenyl)ethanoyl]azepan-4-yl]carbamoyl]butyl]carbamic acid tert-butyl ester 281219-61-2P, [(1S)-1-[(3-Hydroxy-1-phenylcarbamoylazepan-4-yl)carbamoyl]-3-methylbutyl]carbamic acid tert-butyl ester 281219-75-8P, (S)-2-Amino-4-methylpentanoic acid [3-hydroxy-1-(pyridine-2-sulfonyl)azepan-4-yl]amide 281221-08-7P , [(1S)-1-[[1-(3-Chlorobenzenesulfonyl)-3-hydroxyazepan-4-yl]carbamoyl]-3-methylbutyl]carbamic acid tert-butyl ester 281221-10-1P, Benzofuran-2-carboxylic acid [(1S)-1-[[1-(3-chlorobenzenesulfonyl)-3-hydroxyazepan-4-yl]carbamoyl]-3-methylbutyl]amide 281221-46-3P, [(1S)-1-[(3-Hydroxyazepan-4-yl)carbamoyl]-2-cyclohexylethyl]carbamic acid tert-butyl ester 381180-31-0P, [(1S)-1-[[3-Hydroxy-1-(2-fluorophenylcarbamoyl)azepan-4-yl]carbamoyl]-3-methylbutyl]carbamic acid tert-butyl ester 403605-40-3P, [(1S)-1-[(3-Hydroxy-1-phenylsulfonylazepan-4-yl)carbamoyl]-3-methylbutyl]carbamic acid tert-butyl ester 403605-66-3P, (S)-2-Amino-4-methylpentanoic acid [1-(3-chlorobenzenesulfonyl)-3-hydroxyazepan-4-yl]amide 403606-26-8P, [(1S)-1-[(3-Hydroxyazepan-4-yl)carbamoyl]-2-(2-naphthyl)ethyl]carbamic acid tert-butyl ester 403606-29-1P, [(1S)-1-[(3-Hydroxyazepan-4-yl)carbamoyl]-2-phenylethyl]carbamic acid tert-butyl ester 403700-43-6P, [(1S)-1-[(3-Hydroxy-6-methylazepan-4-yl)carbamoyl]-3-methylbutyl]carbamic acid tert-butyl ester 403700-44-7P, 5-((S)-2-[(tert-Butoxycarbonyl)amino]-4-methylpentanoylamino)-6-hydroxy-2-methylazepane-1-carboxylic acid benzyl ester 403700-45-8P, [(1S)-1-[(3-Hydroxy-7-methylazepan-4-yl)carbamoyl]-3-methylbutyl]carbamic acid tert-butyl ester 403700-46-9P, [(1S)-1-[(1-Benzenesulfonyl-3-hydroxy-7-methylazepan-4-yl)carbamoyl]-3-methylbutyl]carbamic acid tert-butyl ester 403700-47-0P, (S)-2-Amino-4-methylpentanoic acid [1-(2-pyridine)sulfonyl-3-hydroxy-7-methylazepan-4-yl]amide 403700-48-1P, Benzofuran-2-carboxylic acid [(1S)-1-[[3-hydroxy-7-methyl-1-(pyridin-2-ylsulfonyl)azepan-4-yl]carbamoyl]-3-methylbutyl]amide
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of 4-aminoazepan-3-one parasitic cysteine protease inhibitors effective against malaria and other diseases)

RN 281219-34-9 ZCAPLUS

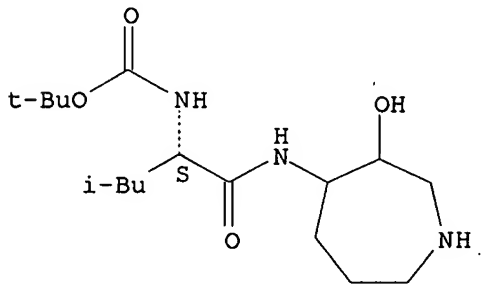
CN 1H-Azepine-1-carboxylic acid, 4-[[(2S)-2-[[(1,1-dimethylethoxy)carbonyl]amino]-4-methyl-1-oxopentyl]amino]hexahydro-3-hydroxy-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



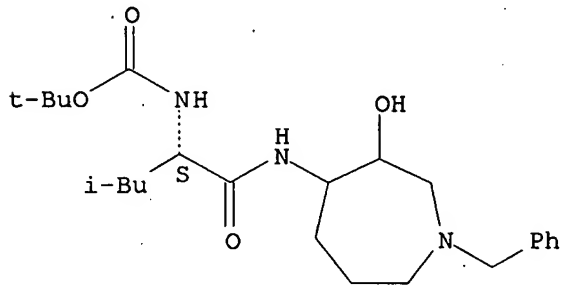
RN 281219-35-0 ZCAPLUS
CN Carbamic acid, [(1S)-1-[[(hexahydro-3-hydroxy-1H-azepin-4-yl)amino]carbonyl]-3-methylbutyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



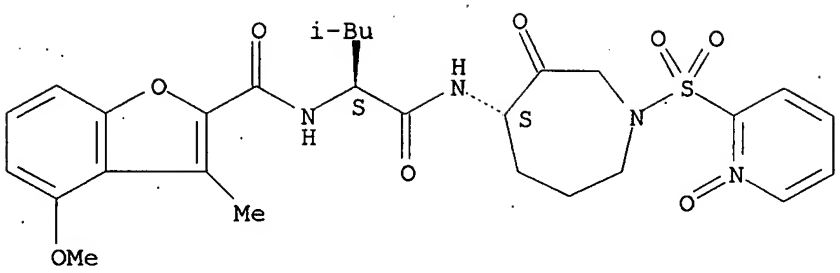
RN 281219-36-1 ZCAPLUS
CN Carbamic acid, [(1S)-1-[[[hexahydro-3-hydroxy-1-(phenylmethyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 281219-37-2 ZCAPLUS
CN Pentanamide, 2-amino-N-[hexahydro-3-hydroxy-1-(phenylmethyl)-1H-azepin-4-yl]-4-methyl-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

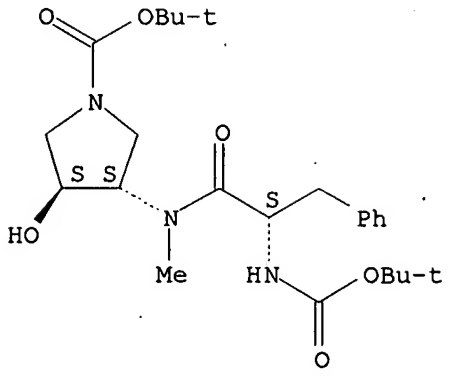
L4 ANSWER 40 OF 76 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:20906 ZCAPLUS
DOCUMENT NUMBER: 136:401599
TITLE: Practical synthesis of (3S,4S)-3-methoxy-4-(methylamino)pyrrolidine
AUTHOR(S): Tsuzuki, Yasunori; Chiba, Katsumi; Mizuno, Kazuhiro; Tomita, Kyoji; Suzuki, Kenji
CORPORATE SOURCE: Dainippon Pharmaceutical Co., Ltd., Chemistry Research Laboratories, Osaka, Suita, 564-0053, Japan
SOURCE: Tetrahedron: Asymmetry (2001), 12(21), 2989-2997
CODEN: TASYE3; ISSN: 0957-4166
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 136:401599

AB Three methods for the preparation of (3S,4S)-3-methoxy-4-(methylamino)pyrrolidine, an important intermediate in the synthesis of the novel quinolone antitumor agent AG-7352, have been developed. By one route an efficient and large-scale preparation of the chiral pyrrolidine could be achieved through resolution of (±)-1-Boc-3-benzylamino-4-hydroxypyrrolidine, which is prepared from either 3-pyrroline or 1,4-dichloro-2-butene.

IT 429673-80-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(practical synthesis of (3S,4S)-3-methoxy-4-(methylamino)pyrrolidine)

RN 429673-80-3 ZCAPLUS
CN 1-Pyrrolidinecarboxylic acid, 3-[[(2S)-2-[[(1,1-dimethylethoxy)carbonyl]amino]-1-oxo-3-phenylpropyl]methylamino]-4-hydroxy-, 1,1-dimethylethyl ester, (3S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 41 OF 76 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:923616 ZCAPLUS
DOCUMENT NUMBER: 136:53691
TITLE: Preparation of 4-amino-azepan-3-one protease inhibitors
INVENTOR(S): Marquis, Robert W., Jr.; Ru, Yu; Veber, Daniel F.; Cummings, Maxwell D.; Thompson, Scott K.; Yamashita, Dennis
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 322 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001095911	A1	20011220	WO 2001-US19062	20010614
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2412353	A1	20011220	CA 2001-2412353	20010614
EP 1307204	A1	20030507	EP 2001-946344	20010614
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HU 200301231	A2	20030828	HU 2003-1231	20010614
JP 2004503502	T	20040205	JP 2002-510089	20010614
BR 2001011693	A	20040406	BR 2001-11693	20010614
NZ 522965	A	20040625	NZ 2001-522965	20010614
BG 107327	A	20030731	BG 2002-107327	20021128
NO 2002005786	A	20030212	NO 2002-5786	20021202
ZA 2002009808	A	20040709	ZA 2002-9808	20021203
IN 2002MN01726	A	20050204	IN 2002-MN1726	20021203
MX 2002PA12442	A	20030425	MX 2002-PA12442	20021213
PRIORITY APPLN. INFO.:			US 2000-593845	A2 20000614

WO 2001-US19062 W 20010614

OTHER SOURCE(S): MARPAT 136:53691

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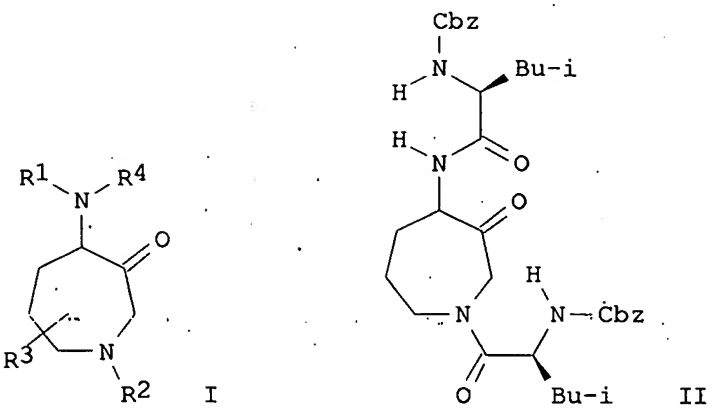


I II

AB The title compds. [I; R1 = COCR13NR11R12, COCR13XR15, COCH2R13; R2 = H, alkyl, cycloalkylalkyl, etc.; R3 = H, alkyl, cycloalkylalkyl, etc.; R4 = H, alkyl, arylalkyl, etc.; R11 = H, alkyl, arylalkyl, etc.; R12 = H, alkyl, cycloalkyl, etc.; R13 = H, alkyl, alkenyl, etc.; R15 = H, alkyl, alkenyl, etc.] which inhibit proteases (no data), including cathepsin K, and are useful for treating diseases of excessive bone loss or cartilage or matrix degradation including osteoporosis, gingival disease including gingivitis and periodontitis, arthritis, more specifically, osteoarthritis and rheumatoid arthritis, Paget's disease, hypercalcemia of malignancy, and metabolic bone disease, were prepared E.g., a multi-step synthesis of compound II was given.

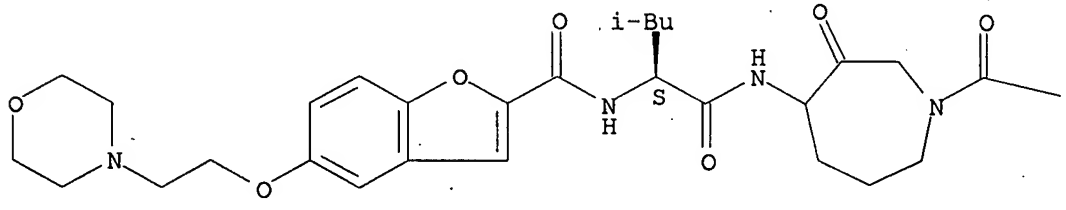
IT 281214-81-1P 281214-85-5P 281214-88-8P
281214-92-4P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of 4-amino-azepan-3-one protease inhibitors)

RN 281214-81-1 ZCAPLUS

CN 1H-Azepine-1-carboxylic acid, hexahydro-4-[[(2S)-4-methyl-2-[[[5-[2-(4-morpholinyl)ethoxy]-2-benzofuranyl]carbonyl]amino]-1-oxopentyl]amino]-3-oxo-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

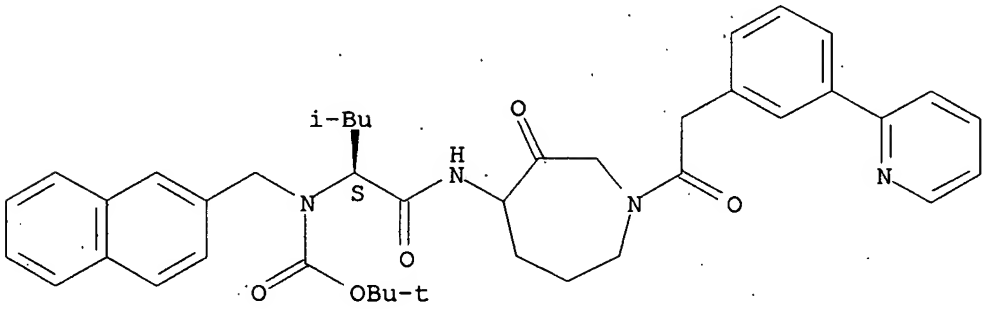


PAGE 1-B

—OBu-t

RN 281214-85-5 ZCAPLUS
CN Carbamic acid, [(1S)-1-[[[hexahydro-3-oxo-1-[[3-(2-pyridinyl)phenyl]acetyl]-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl](2-naphthalenylmethyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

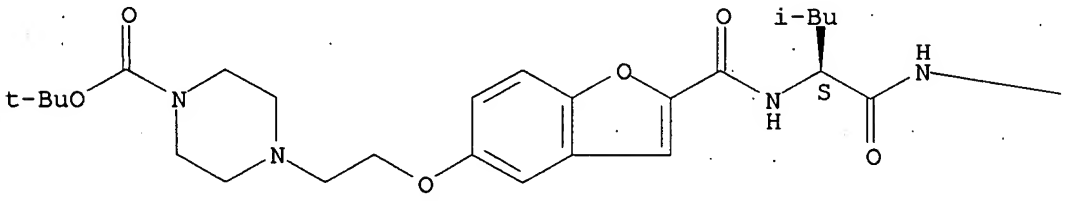
Absolute stereochemistry.



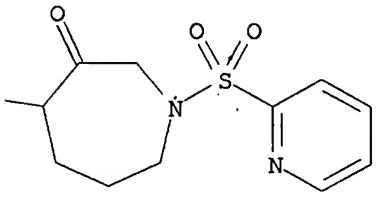
RN 281214-88-8 ZCAPLUS
CN 1-Piperazinecarboxylic acid, 4-[2-[[2-[[[(1S)-1-[[[hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]amino]carbonyl]-5-benzofuranyl]oxy]ethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

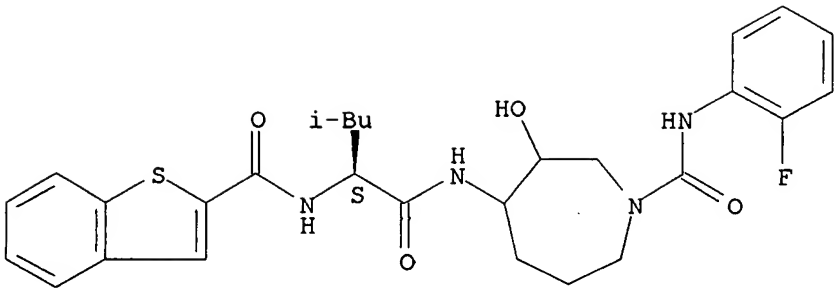
PAGE 1-A



PAGE 1-B



RN 281214-92-4 ZCAPLUS
CN 1-Piperazinecarboxylic acid, 4-[2-[[2-[[[(1S)-1-[[[hexahydro-3-oxo-1-[2-[3-



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 42 OF 76 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:868156 ZCAPLUS
DOCUMENT NUMBER: 136:6349
TITLE: Preparation of 4-aminoazepan-3-one derivatives as protease inhibitors
INVENTOR(S): Cummings, Maxwell D.; Marquis, Robert W., Jr.; Ru, Yu; Thompson, Scott K.; Veber, Daniel F.; Yamashita, Dennis S.
PATENT ASSIGNEE(S): SmithKline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 95 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001089451	A2	20011129	WO 2001-US12326	20010417
WO 2001089451	A3	20020404		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2406829	A1	20011129	CA 2001-2406829	20010417
AU 200190507	A	20011203	AU 2001-90507	20010417
EP 1278502	A2	20030129	EP 2001-970508	20010417
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
HU 200301781	A2	20030929	HU 2003-1781	20010417
JP 2004526662	T	20040902	JP 2001-585697	20010417
BR 2001008954	A	20060509	BR 2001-8954	20010417
IN 2002MN01041	A	20050304	IN 2002-MN1041	20020731
ZA 2002007872	A	20050606	ZA 2002-7872	20021001
NO 2002005005	A	20021206	NO 2002-5005	20021017
MX 2002PA10276	A	20030425	MX 2002-PA10276	20021017
US 2003114437	A1	20030619	US 2002-258053	20021017
US 2004229863	A1	20041118	US 2004-797828	20040310
PRIORITY APPLN. INFO.:			US 2000-198493P P	20000418
			US 2001-273811P P	20010307

WO 2001-US12326 W 20010417
US 2002-258053 B1 20021017

OTHER SOURCE(S): MARPAT 136:6349

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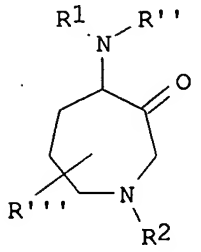


I

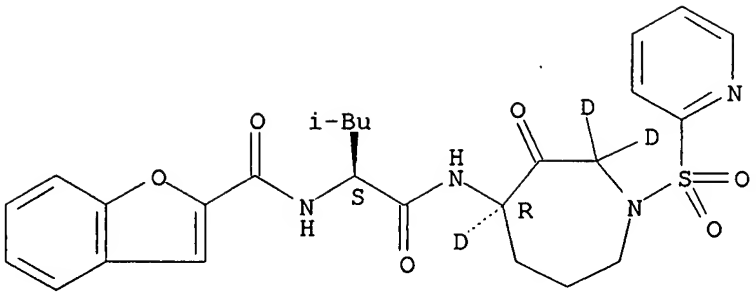
AB 4-Aminoazepan-3-one derivs. I [R1 is an acyl group R3CH2CO, R4NR'CHR3CO or R5-X-CHR3CO; R2-R5 = H, alkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, etc.; R', R'' = H, alkyl, aryl, arylalkyl, heterocyclyl, heterocyclylalkyl; X = CH2, S or O; R''' = cycloalkyl, cycloalkyl or any group given for R' and R''; R3 and R' may be connected to form a pyrrolidine, piperidine or morpholine ring] or their pharmaceutically acceptable salts were prepared as protease inhibitors, particularly cathepsin S, for treating various diseases. Thus, benzofuran-2-carboxylic acid [(S)-2-cyclohexyl-1-[3-oxo-1-(pyridine-2-sulfonyl)azepan-4-ylcarbamoyl]ethyl]amide was prepared by a multistep procedure involving coupling of 4-amino-1-(pyridine-2-sulfonyl)azepan-3-ol (preparation given) with N-Boc-cyclohexylalanine (Boc = tert-butoxycarbonyl), deprotection, coupling with benzofuran-2-carboxylic acid, and oxidation with Dess-Martin reagent.

IT 281216-44-2P 281216-47-5P 281217-02-5P
281217-03-6P 281217-05-8P 281217-06-9P
281217-08-1P 281218-50-6P 281218-53-9P
281219-04-3P 281219-06-5P 281219-08-7P
281219-09-8P 281219-10-1P 362506-61-4P
362506-64-7P 362506-67-0P 362506-70-5P
362506-72-7P 362506-74-9P 362506-76-1P
362506-82-9P 362506-85-2P 362506-88-5P
375813-32-4P 375813-33-5P 375813-34-6P
375813-35-7P 375813-36-8P 375813-38-0P
375813-39-1P 375813-40-4P 375813-41-5P
375813-42-6P 375813-43-7P 375813-44-8P
375813-46-0P 375813-48-2P 375813-49-3P
375813-50-6P 375813-52-8P 375813-54-0P
375813-56-2P 375813-57-3P 375813-59-5P
375813-60-8P 375813-62-0P 375813-64-2P
375813-66-4P 375813-68-6P 375813-70-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of aminoazepanone cyclohexyalanine derivs. as protease inhibitors)

RN 281216-44-2 ZCAPLUS

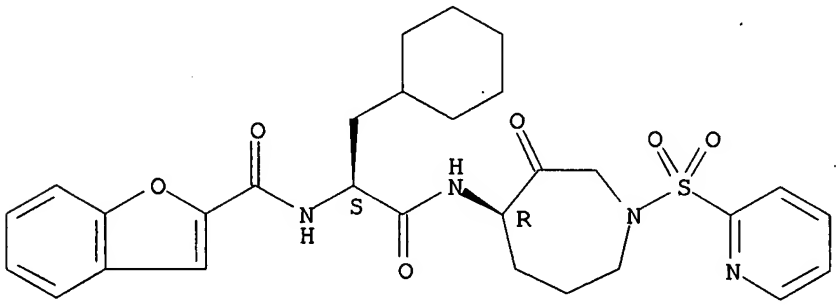
CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[(4R)-hexahydro-2,4-d2-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl-2-d]amino]carbonyl]-3-methylbutyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



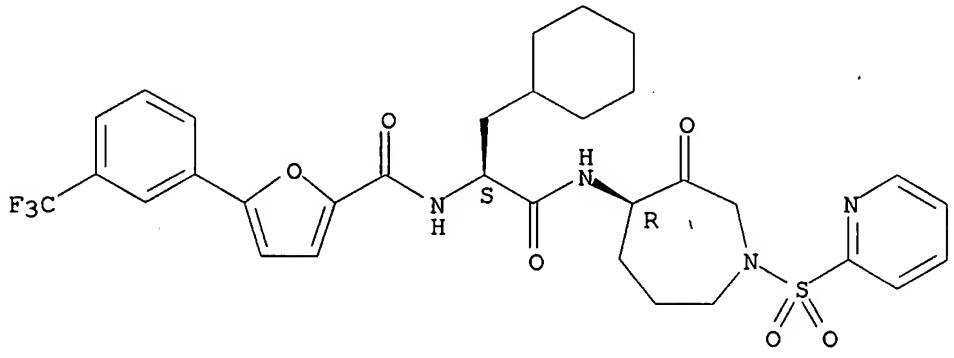
RN 281216-47-5 ZCAPLUS
CN 2-Benzofurancarboxamide, N-[(1S)-1-(cyclohexylmethyl)-2-[[(4R)-hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



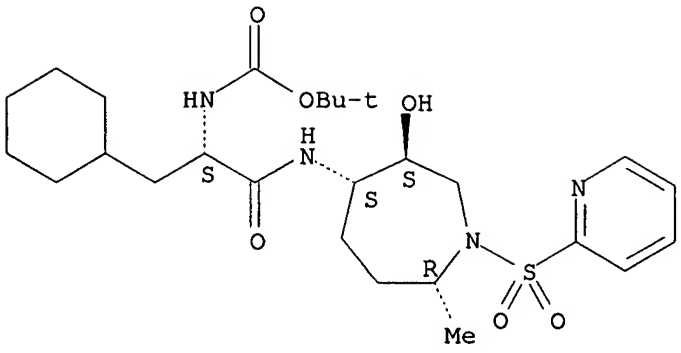
RN 281217-02-5 ZCAPLUS
CN 2-Furancarboxamide, N-[(1S)-1-(cyclohexylmethyl)-2-[[(4R)-hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]-2-oxoethyl]-5-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



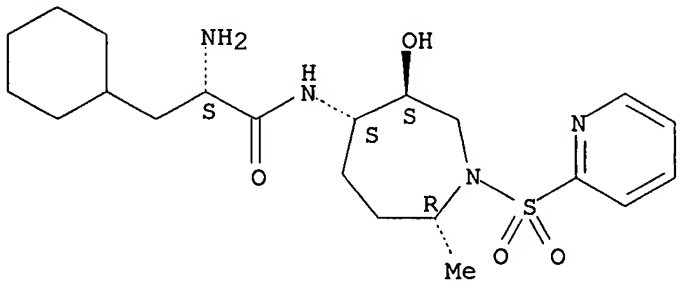
RN 281217-03-6 ZCAPLUS
CN 2-Furancarboxamide, 5-(4-chlorophenyl)-N-[(1S)-1-(cyclohexylmethyl)-2-[[(4R)-hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 375813-86-8 ZCAPLUS
CN Cyclohexanepropanamide, α-amino-N-[(3S,4S,7R)-hexahydro-3-hydroxy-7-methyl-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-, (αS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 43 OF 76 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:780691 ZCAPLUS
DOCUMENT NUMBER: 135:327371
TITLE: 4-Amino-azepan-3-one inhibitors of cathepsin L, their preparation, and their therapeutic use
INVENTOR(S): Cummings, Maxwell D.; Marquis, Robert W., Jr.; Ru, Yu; Thompson, Scott K.; Veber, Daniel F.; Yamashita, Dennis S.
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001078734	A1	20011025	WO 2001-US12386	20010417

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, BY
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,

DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1303281	A1	20030423	EP 2001-927076	20010417
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003531122	T	20031021	JP 2001-576034	20010417
US 2004034013	A1	20040219	US 2002-258412	20021017
PRIORITY APPLN. INFO.:			US 2000-197717P	P 20000418
			WO 2001-US12386	W 20010417

OTHER SOURCE(S): MARPAT 135:327371

AB Methods are provided which use 4-amino-azepan-3-one protease inhibitors of cathepsin L in the treatment of diseases in which cathepsin L is implicated, especially treatment or prevention of rheumatoid arthritis; cancer metastasis; diseases requiring inhibition of tissue destruction by macrophages, particularly lung macrophages, such as asthma, chronic obstructive pulmonary disease (COPD), and emphysema; and diseases requiring therapy; inhibition of pos. selection of CD4+T- cells by cortical thymic epithelial cells.

IT 281215-01-8P

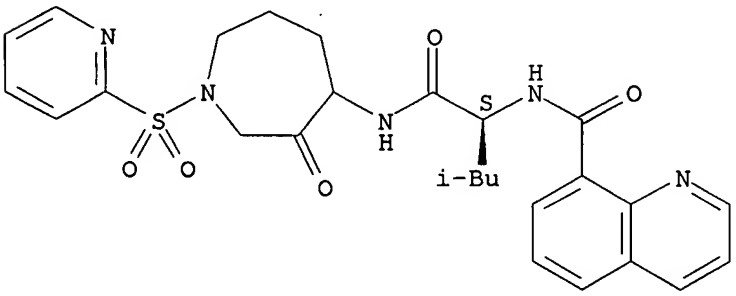
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(aminoazepanone inhibitors of cathepsin L, preparation, and therapeutic use)

RN 281215-01-8 ZCAPLUS

CN 8-Quinolinecarboxamide, N-[(1S)-1-[[[hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 281215-03-0P 281215-06-3P 281216-55-5P
281217-10-5P 281217-11-6P 281217-12-7P
281217-14-9P 281217-22-9P 281217-50-3P
281217-52-5P 281218-61-9P 281219-14-5P
369593-17-9P 369593-18-0P 369593-19-1P
369593-20-4P 369593-21-5P 369593-22-6P

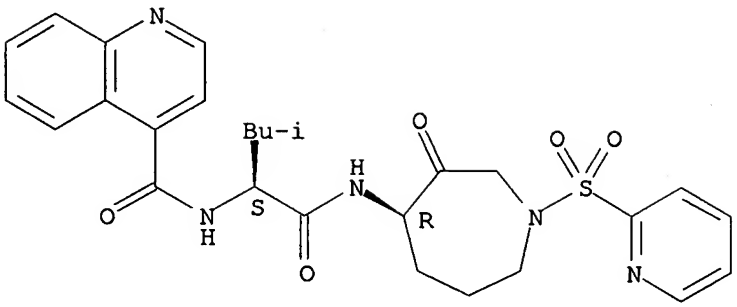
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(aminoazepanone inhibitors of cathepsin L, preparation, and therapeutic use)

RN 281215-03-0 ZCAPLUS

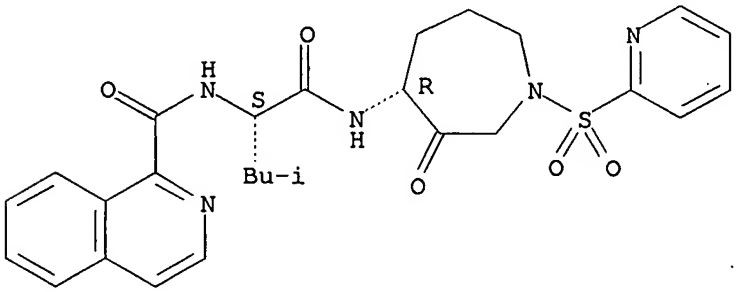
CN 4-Quinolinecarboxamide, N-[(1S)-1-[[[(4R)-hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



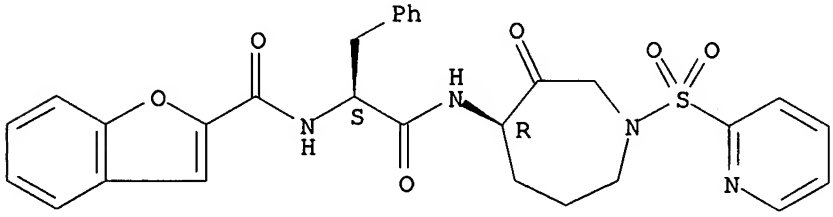
RN 281215-06-3 ZCAPLUS
CN 1-Isoquinolinecarboxamide, N-[(1S)-1-[[[(4R)-hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



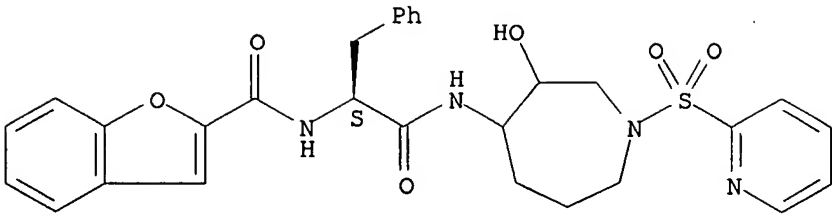
RN 281216-55-5 ZCAPLUS
CN 2-Benzofurancarboxamide, N-[(1S)-2-[[(4R)-hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]-2-oxo-1-(phenylmethyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 281217-10-5 ZCAPLUS
CN 8-Quinolinecarboxamide, N-[(1S)-2-[[hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]-1-(2-naphthalenylmethyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 44 OF 76 ZCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:746949 ZCAPLUS
DOCUMENT NUMBER: 136:395726

TITLE: Potent and selective inhibition of human cathepsin K leads to inhibition of bone resorption in vivo in a nonhuman primate

AUTHOR(S): Stroup, George B.; Lark, Michael W.; Veber, Daniel F.; Bhattacharyya, Amit; Blake, Simon; Dare, Lauren C.; Erhard, Karl F.; Hoffman, Sandra J.; James, Ian E.; Marquis, Robert W.; Ru, Yu; Vasko-Moser, Janice A.; Smith, Brian R.; Tomaszek, Thadeus; Gowen, Maxine
CORPORATE SOURCE: Department of Bone and Cartilage Biology, SmithKline Beecham Pharmaceuticals, King of Prussia, PA, USA

SOURCE: Journal of Bone and Mineral Research (2001), 16(10), 1739-1746
CODEN: JBMREJ; ISSN: 0884-0431
PUBLISHER: American Society for Bone and Mineral Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Cathepsin K is a cysteine protease that plays an essential role in osteoclast-mediated degradation of the organic matrix of bone. Knockout of the enzyme in mice, as well as lack of functional enzyme in the human condition pycnodysostosis, results in osteopetrosis. These results suggests that inhibition of the human enzyme may provide protection from bone loss in states of elevated bone turnover, such as postmenopausal osteoporosis. To test this theory, we have produced a small mol. inhibitor of human cathepsin K, SB-357114, that potently and selectively inhibits this enzyme (Ki = 0.16 nM). This compound potently inhibited cathepsin activity in situ, in human osteoclasts (inhibitor concentration [IC]50 = 70 nM) as well as bone resorption mediated by human osteoclasts in vitro (IC50 = 29 nM). Using SB-357114, we evaluated the effect of inhibition of cathepsin K on bone resorption in vivo using a nonhuman primate model of postmenopausal bone loss in which the active form of cathepsin K is identical to the human orthologue. A gonadotropin-releasing hormone agonist (GnRHa) was used to render cynomolgus monkeys estrogen deficient, which led to an increase in bone turnover. Treatment with SB-357114 (12 mg/kg s.c.) resulted in a significant reduction in serum markers of bone resorption relative to untreated controls. The effect was observed 1.5 h after the first dose and was maintained for 24 h. After 5 days of dosing, the redns. in N-terminal telopeptides (NTx) and C-terminal telopeptides (CTx) of type I collagen were 61% and 67%, resp. A decrease in serum osteocalcin of 22% was also observed These data show that inhibition of cathepsin K results in a significant reduction of bone resorption in vivo and provide further evidence that this may be a viable approach to the treatment of postmenopausal osteoporosis.

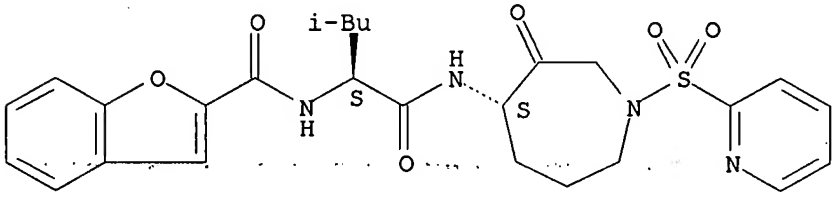
IT 281217-45-6, SB 357114

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cathepsin K inhibitor leads to inhibition of bone resorption)

RN 281217-45-6 ZCAPLUS

CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[(4S)-hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 45 OF 76 ZCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:713145 ZCAPLUS

DOCUMENT NUMBER: 135:273219

TITLE: Preparation of C1-6 alkyl-4-aminoazepan-3-one derivatives as protease inhibitors

INVENTOR(S): Cummings, Maxwell D.; Marquis, Robert W., Jr.; Ru, Yu; Thompson, Scott K.; Veber, Daniel F.; Yamashita, Dennis S.

PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA

SOURCE: PCT Int. Appl., 173 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

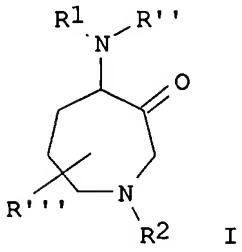
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001070232	A1	20010927	WO 2001-US7094	20010307
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, BY				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2404206	A1	20010927	CA 2001-2404206	20010307
EP 1307203	A1	20030507	EP 2001-916412	20010307
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
HU 200300068	A2	20030528	HU 2003-68	20010307
BR 2001009356	A	20030603	BR 2001-9356	20010307
JP 2003527429	T	20030916	JP 2001-568430	20010307
NZ 520588	A	20040625	NZ 2001-520588	20010307
AP 1540	A	20060228	AP 2002-2593	20010307
W: GM, GH, KE, LS, MW, MZ, SL, SD, SZ, TZ, UG, ZM, ZW				
BG 106962	A	20030331	BG 2002-106962	20020729

IN 2002MN01040	A	20050304	IN 2002-MN1040		20020731
ZA 2002007478	A	20031008	ZA 2002-7478		20020918
NO 2002004528	A	20021119	NO 2002-4528		20020920
US 2004044201	A1	20040304	US 2002-239343		20020920
US 7071184	B2	20060704			
US 2006194787	A1	20060831	US 2006-410558		20060425
PRIORITY APPLN. INFO.:			US 2000-191000P	P	20000321
			US 2000-206341P	P	20000523
			US 2000-211759P	P	20000614
			US 2000-217445P	P	20000710
			WO 2001-US7094	W	20010307
			US 2002-239343	A1	20020920

OTHER SOURCE(S): MARPAT 135:273219

GI



I

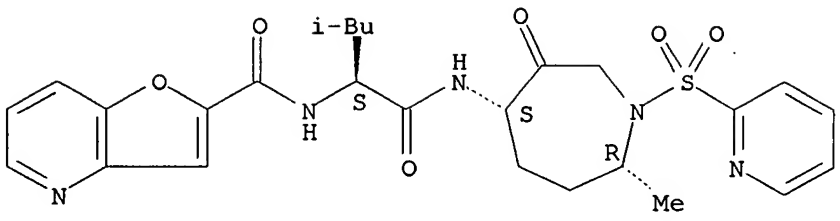
AB 4-Aminoazepan-3-one derivs. I [R1 is an acyl group R3CH2CO, R4NR'CRR3CO or R5-X-CHR3CO; R = H or RR3 = (CH2)n (n = 1-5); R2-R5 = H, alkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, etc.; R', R'' = H, alkyl, aryl, arylalkyl, heterocyclyl, heterocyclylalkyl; X = CH2, S or O; R''' = alkyl; R3 and R' may be connected to form a pyrrolidine, piperidine or morpholine ring] or their pharmaceutically acceptable salts were prepared as protease inhibitors for treating various diseases, including excessive bone loss or cartilage or matrix degradation Thus, 5-methoxybenzofuran-2-carboxylic acid [(S)-3-methyl-1-[(4S,6S)- (or 4R,6R)-6-methyl-3-oxo-1-(pyridine-2-sulfonyl)azepan-4-ylcarbamoyl]butyl]amide was prepared by a multistep procedure involving coupling of 4-amino-6-methyl-1-(pyridine-2-sulfonyl)azepan-3-ol (preparation given) with Boc-Leu-OH and 5-methoxybenzofuran-2-carboxylic acid.

IT 362505-90-6P 362507-09-3P 362507-77-5P
362507-81-1P 362508-75-6P 362508-93-8P
362509-05-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of alkyl aminoazepanone derivs. as protease inhibitors)

RN 362505-90-6 ZCAPLUS

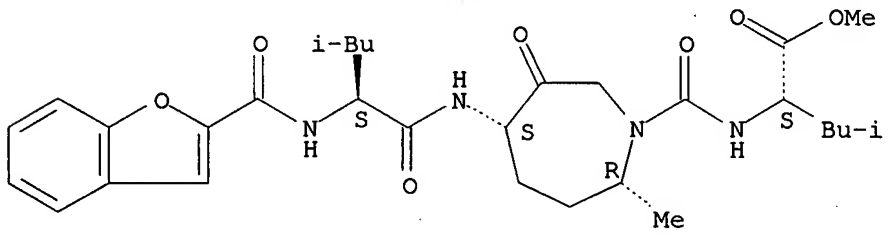
CN Furo[3,2-b]pyridine-2-carboxamide, N-[(1S)-1-[[[(4S,7R)-hexahydro-7-methyl-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



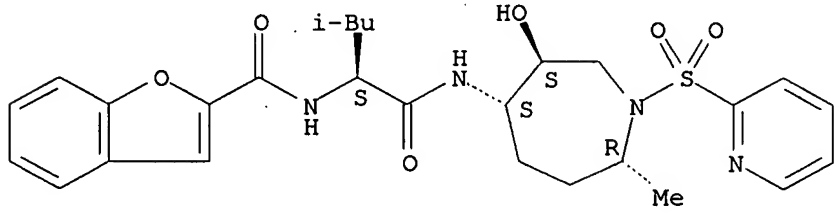
RN 362507-09-3 ZCAPLUS
CN L-Leucine, N-(2-benzofuranylcarbonyl)-L-leucyl-(2R,5S)-5-aminohexahydro-2-methyl-6-oxo-1H-azepine-1-carbonyl-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



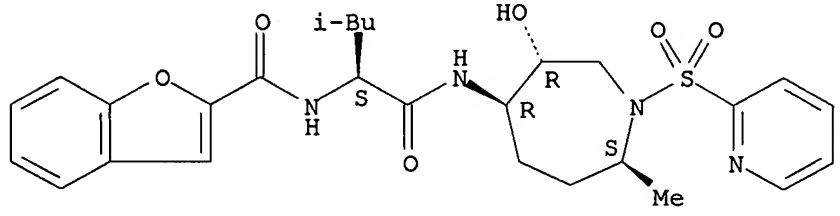
RN 362507-77-5 ZCAPLUS
CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[(3S,4S,7R)-hexahydro-3-hydroxy-7-methyl-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 362507-81-1 ZCAPLUS
CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[(3R,4R,7S)-hexahydro-3-hydroxy-7-methyl-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

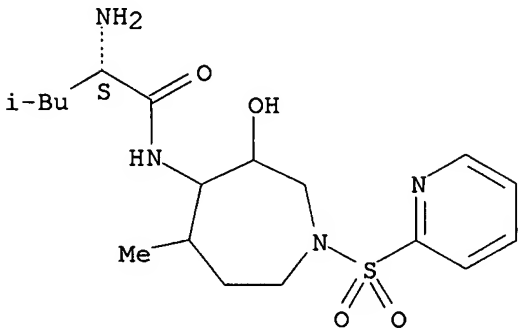
Absolute stereochemistry.



RN 362508-75-6 ZCAPLUS
CN 2-Furancarboxamide, N-[(1S)-1-(cyclohexylmethyl)-2-[[(3S,4S,7R)-hexahydro-3-hydroxy-7-methyl-1-propyl-1H-azepin-4-yl]amino]-2-oxoethyl]- (9CI) (CA

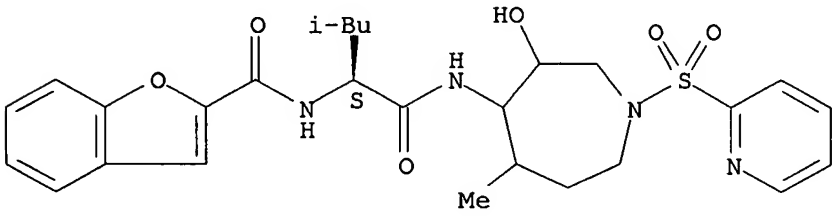
pyridinylsulfonyl)-1H-azepin-4-yl]-4-methyl-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 362632-43-7 ZCAPLUS
CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[hexahydro-3-hydroxy-5-methyl-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 46 OF 76 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:359993 ZCAPLUS
DOCUMENT NUMBER: 134:353552
TITLE: Preparation of leucine 4-aminoazepan-3-one derivatives as protease inhibitors
INVENTOR(S): Marquis, Robert Wells, Jr.; Veber, Daniel Frank
PATENT ASSIGNEE(S): SmithKline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001034600	A1	20010517	WO 2000-US30757	20001108
W: CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
EP 1232154	A1	20020821	EP 2000-977089	20001108
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR				
JP 2003513972	T	20030415	JP 2001-536547	20001108
US 6583137	B1	20030624	US 2002-129674	20020506

PRIORITY APPLN. INFO.: US 1999-164560P P 19991110
WO 2000-US30757 W 20001108

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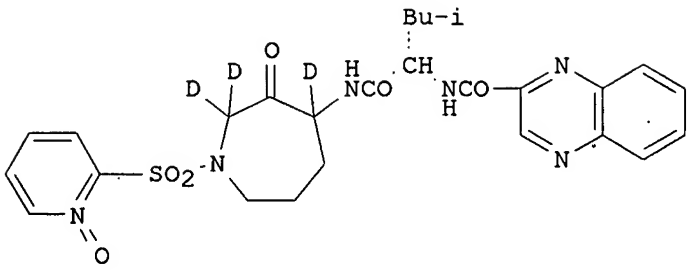


I

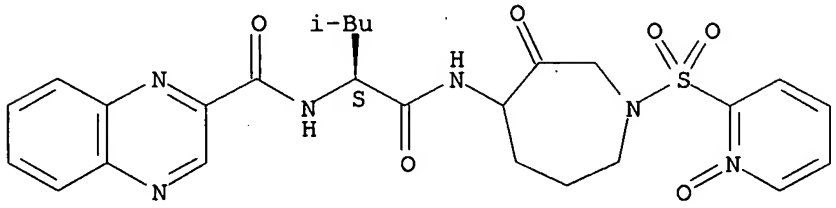
AB 2-Quinoxalinecarboxylic acid amide I or a pharmaceutically acceptable salt, hydrate or solvate was prepared as an inhibitor of cysteine proteases, particularly cathepsin K, and is useful in the treatment of diseases in which inhibition of bone loss or of cartilage degradation is a factor. Thus, 4-amino-3-hydroxyazepane-1-carboxylic acid benzyl ester (preparation given) underwent sequential coupling with Boc-Leu-OH, catalytic hydrogenolysis, sulfonylation with 2-pyridinesulfonyl chloride N-oxide, Boc-deprotection, acylation with 2-quinoxalinecarboxylic acid, hydroxyl group oxidation with pyridine-sulfur trioxide, and deuteration to afford I as a mixture of diastereomers which was separated by HPLC.

IT 339290-80-1P 339290-81-2P 339290-82-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of leucine aminoazepanone derivs. as protease inhibitors)

RN 339290-80-1 ZCAPLUS

CN 2-Quinoxalinecarboxamide, N-[(1S)-1-[[[hexahydro-1-[(1-oxido-2-pyridinyl)sulfonyl]-3-oxo-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

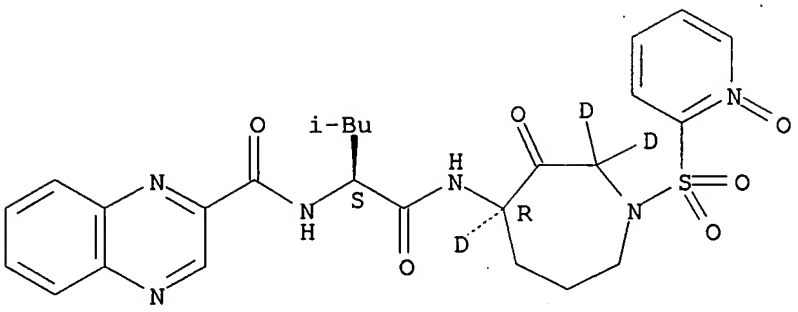
Absolute stereochemistry.



RN 339290-81-2 ZCAPLUS

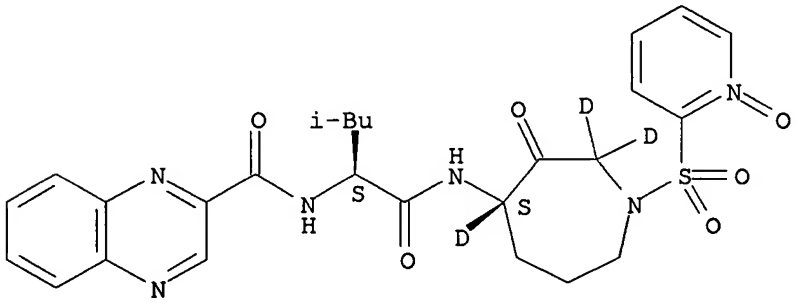
CN 2-Quinoxalinecarboxamide, N-[(1S)-1-[[[(4R)-hexahydro-2,4-d2-1-[(1-oxido-2-pyridinyl)sulfonyl]-3-oxo-1H-azepin-4-yl-2-d]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



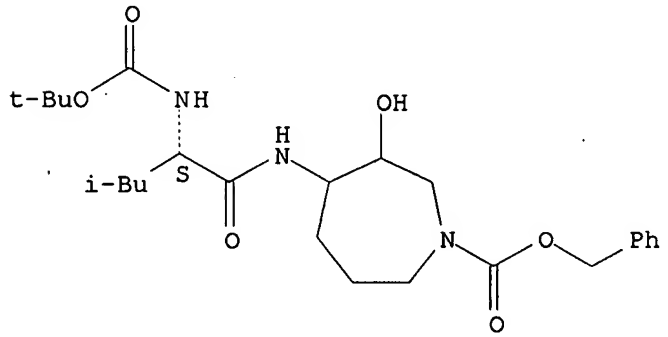
RN 339290-82-3 ZCAPLUS
CN 2-Quinoxalinecarboxamide, N-[(1S)-1-[[[(4S)-hexahydro-2,4-d2-1-[(1-oxido-2-pyridinyl)sulfonyl]-3-oxo-1H-azepin-4-yl-2-d]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 281219-34-9P 281219-35-0P 281220-55-1P
281220-56-2P 281220-74-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of leucine aminoazepanone derivs. as protease inhibitors)
RN 281219-34-9 ZCAPLUS
CN 1H-Azepine-1-carboxylic acid, 4-[[(2S)-2-[[(1,1-dimethylethoxy)carbonyl]amino]-4-methyl-1-oxopentyl]amino]hexahydro-3-hydroxy-, phenylmethyl ester (9CI) (CA INDEX NAME)

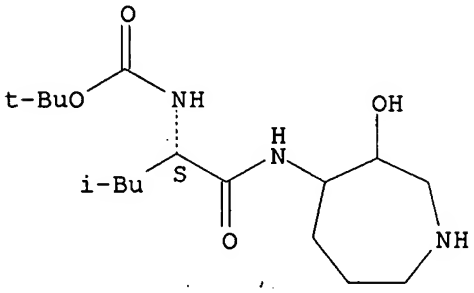
Absolute stereochemistry.



RN 281219-35-0 ZCAPLUS

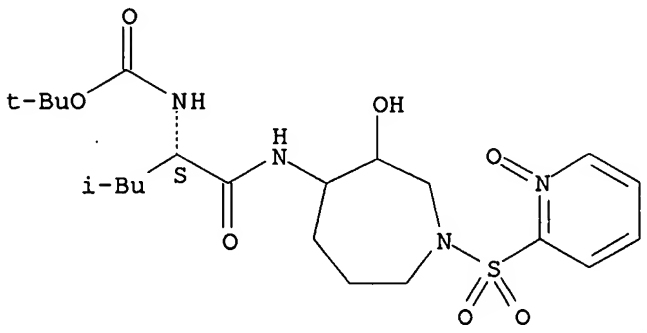
CN Carbamic acid, [(1S)-1-[[(hexahydro-3-hydroxy-1H-azepin-4-yl)amino]carbonyl]-3-methylbutyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



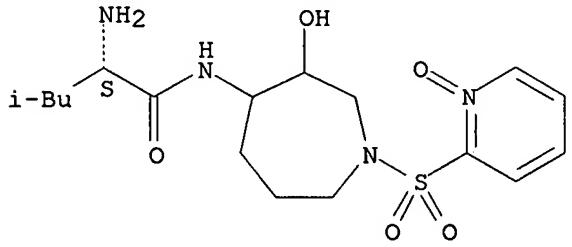
RN 281220-55-1 ZCAPLUS
CN Carbamic acid, [(1S)-1-[[[hexahydro-3-hydroxy-1-[(1-oxido-2-pyridinyl)sulfonyl]-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



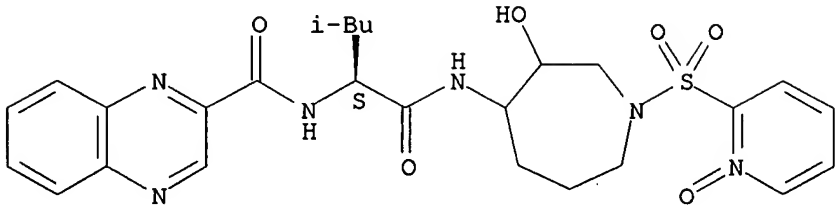
RN 281220-56-2 ZCAPLUS
CN Pentanamide, 2-amino-N-[hexahydro-3-hydroxy-1-[(1-oxido-2-pyridinyl)sulfonyl]-1H-azepin-4-yl]-4-methyl-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 281220-74-4 ZCAPLUS
CN 2-Quinoxalinecarboxamide, N-[(1S)-1-[[[hexahydro-3-hydroxy-1-[(1-oxido-2-pyridinyl)sulfonyl]-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 47 OF 76 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:359992 ZCAPLUS
DOCUMENT NUMBER: 134:353551
TITLE: Preparation of leucine 4-aminoazepan-3-one derivatives as protease inhibitors
INVENTOR(S): Marquis, Robert W., Jr.; Veber, Daniel Frank
PATENT ASSIGNEE(S): SmithKline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2001034599	A1	20010517	WO 2000-US30685		20001108
W: AU, CA, JP, US					
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR					
EP 1232155	A1	20020821	EP 2000-978423		20001108
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR					
JP 2003513971	T	20030415	JP 2001-536546		20001108
US 6596715	B1	20030722	US 2002-129671		20020506
PRIORITY APPLN. INFO.:			US 1999-164634P	P	19991110
			WO 2000-US30685	W	20001108

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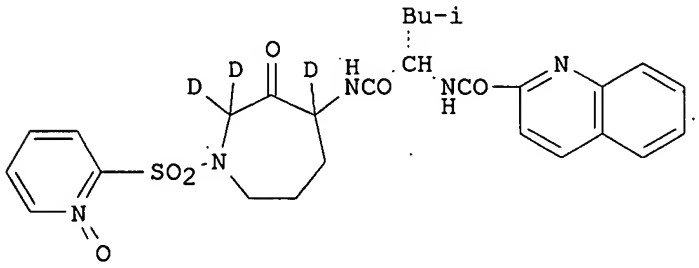


I

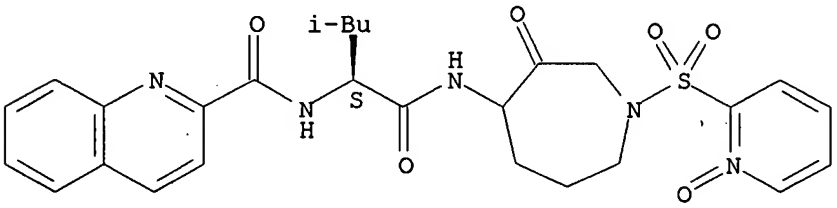
AB 2-Quinolinecarboxylic acid amide I or a pharmaceutically acceptable salt, hydrate or solvate was prepared as an inhibitor of cysteine proteases, particularly cathepsin K, and is useful in the treatment of diseases in which inhibition of bone loss or of cartilage degradation is a factor. Thus, 4-amino-3-hydroxyazepane-1-carboxylic acid benzyl ester (preparation given)

underwent sequential coupling with Boc-Leu-OH, catalytic hydrogenolysis, sulfonylation with 2-pyridinesulfonyl chloride N-oxide, Boc-deprotection, acylation with 2-quinolinecarboxylic acid, hydroxyl group oxidation with pyridine-sulfur trioxide, and deuteration to afford I as a mixture of diastereomers which was separated by HPLC.

IT 339286-06-5P 339286-08-7P 339286-09-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of leucine aminoazepanone derivs. as protease inhibitors)

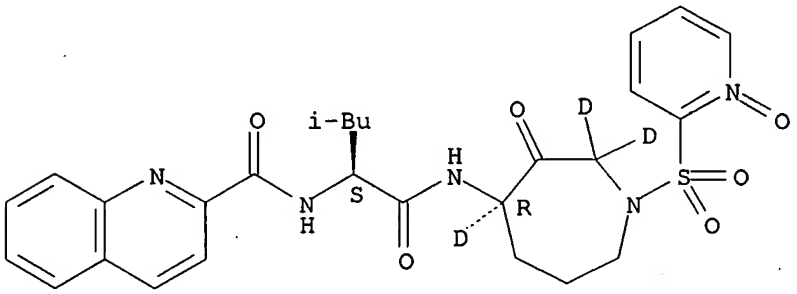
RN 339286-06-5 ZCAPLUS
CN 2-Quinolinecarboxamide, N-[(1S)-1-[[[hexahydro-1-[(1-oxido-2-pyridinyl)sulfonyl]-3-oxo-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



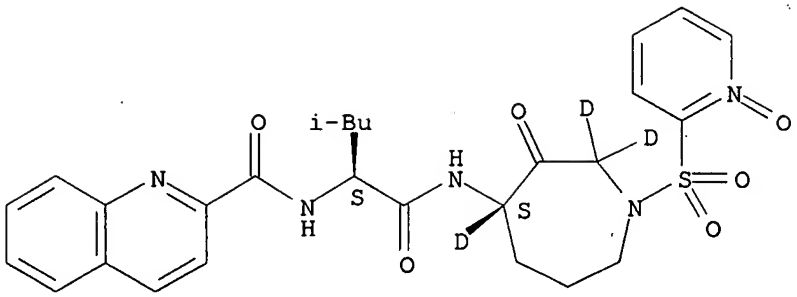
RN 339286-08-7 ZCAPLUS
CN 2-Quinolinecarboxamide, N-[(1S)-1-[[[(4R)-hexahydro-2,4-d2-1-[(1-oxido-2-pyridinyl)sulfonyl]-3-oxo-1H-azepin-4-yl-2-d]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 339286-09-8 ZCAPLUS
CN 2-Quinolinecarboxamide, N-[(1S)-1-[[[(4S)-hexahydro-2,4-d2-1-[(1-oxido-2-pyridinyl)sulfonyl]-3-oxo-1H-azepin-4-yl-2-d]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

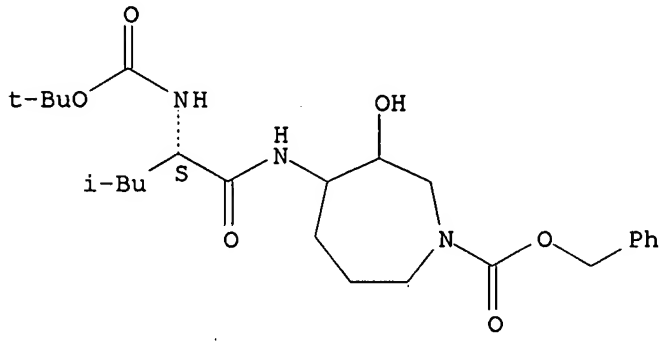
Absolute stereochemistry.



IT 281219-34-9P 281219-35-0P 281220-55-1P
281220-56-2P 281220-75-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of leucine aminoazepanone derivs. as protease inhibitors)

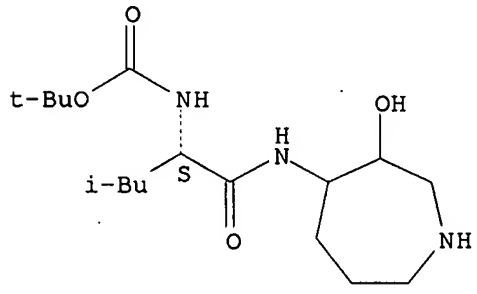
RN 281219-34-9 ZCAPLUS
CN 1H-Azepine-1-carboxylic acid, 4-[[(2S)-2-[[(1,1-dimethylethoxy)carbonyl]amino]-4-methyl-1-oxopentyl]amino]hexahydro-3-hydroxy-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 281219-35-0 ZCAPLUS
CN Carbamic acid, [(1S)-1-[[(hexahydro-3-hydroxy-1H-azepin-4-yl)amino]carbonyl]-3-methylbutyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

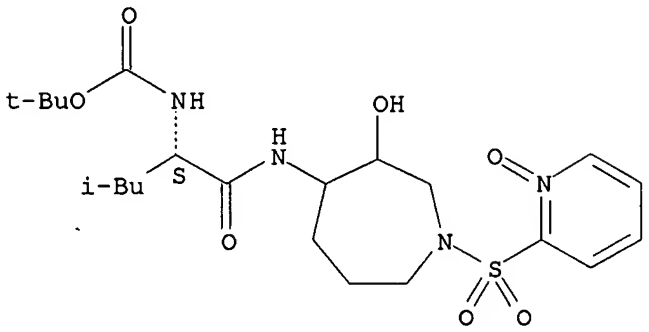
Absolute stereochemistry.



RN 281220-55-1 ZCAPLUS
CN Carbamic acid, [(1S)-1-[[[hexahydro-3-hydroxy-1-[(1-oxido-2-pyridinyl)sulfonyl]-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]-,

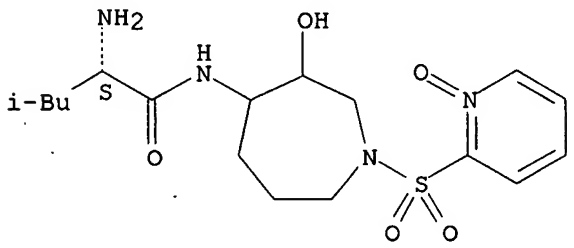
1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



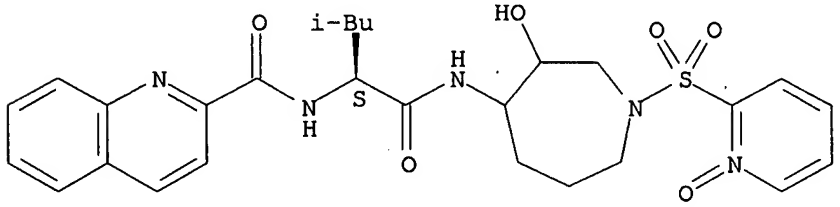
RN 281220-56-2 ZCAPLUS
CN Pentanamide, 2-amino-N-[hexahydro-3-hydroxy-1-[(1-oxido-2-pyridinyl)sulfonyl]-1H-azepin-4-yl]-4-methyl-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 281220-75-5 ZCAPLUS
CN 2-Quinolinecarboxamide, N-[(1S)-1-[[[hexahydro-3-hydroxy-1-[(1-oxido-2-pyridinyl)sulfonyl]-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 48 OF 76 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:359961 ZCAPLUS
DOCUMENT NUMBER: 134:353550
TITLE: Preparation of leucine 4-aminoazepan-3-one derivatives as protease inhibitors
INVENTOR(S): Marquis, Robert W., Jr.; Veber, Daniel Frank
PATENT ASSIGNEE(S): SmithKline Beecham Corporation, USA

SOURCE: PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001034566	A2	20010517	WO 2000-US30682	20001108
WO 2001034566	A3	20030731		
W: AU, CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
AU 2001014747	A5	20010606	AU 2001-14747	20001108
EP 1351930	A2	20031015	EP 2000-977056	20001108
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR				
JP 2003533432	T	20031111	JP 2001-536515	20001108

PRIORITY APPLN. INFO.: US 1999-164561P P 19991110
WO 2000-US30682 W 20001108

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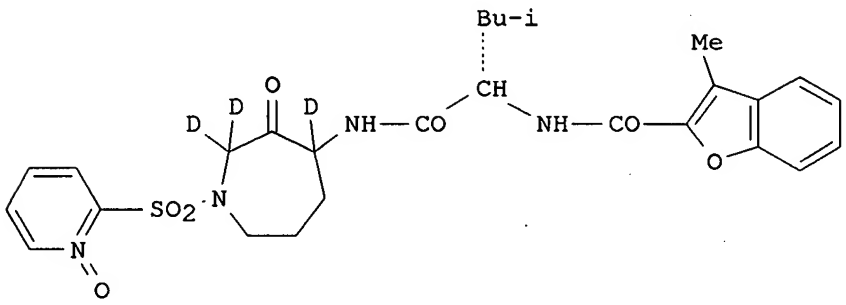


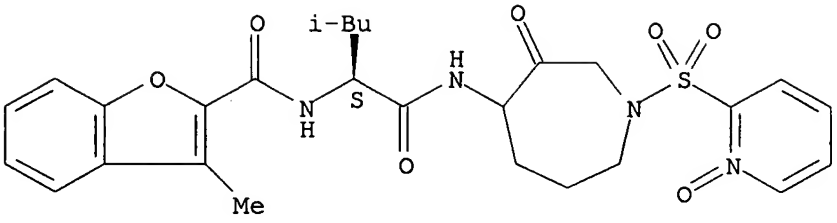
AB 3-Methylbenzofuran-2-carboxylic acid amide I or a pharmaceutically acceptable salt, hydrate or solvate was prepared as an inhibitor of cysteine proteases, particularly cathepsin K, and is useful in the treatment of diseases in which inhibition of bone loss or of cartilage degradation is a factor. Thus, 4-amino-3-hydroxyazepane-1-carboxylic acid benzyl ester (preparation given) underwent sequential coupling with Boc-Leu-OH, catalytic hydrogenolysis, sulfonylation with 2-pyridinesulfonyl chloride N-oxide, Boc-deprotection, acylation with 3-methylbenzofuran-2-carboxylic acid, hydroxyl group oxidation with pyridine-sulfur trioxide, and deuteration to afford I as a mixture of diastereomers which was separated by HPLC.

IT 339269-37-3P 339269-38-4P 339269-39-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of leucine aminoazepanone derivs. as protease inhibitors)

RN 339269-37-3 ZCAPLUS

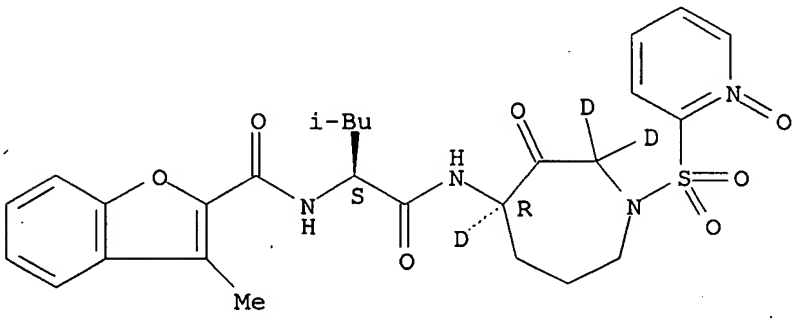
CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[hexahydro-1-[(1-oxido-2-pyridinyl)sulfonyl]-3-oxo-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]-3-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



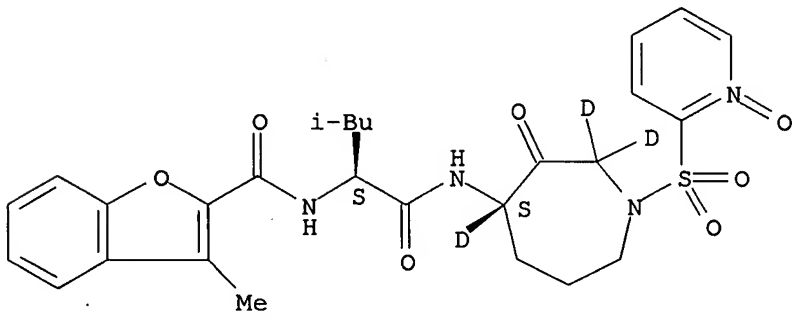
RN 339269-38-4 ZCAPLUS
CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[(4R)-hexahydro-2,4-d2-1-[(1-oxido-2-pyridinyl)sulfonyl]-3-oxo-1H-azepin-4-yl-2-d]amino]carbonyl]-3-methylbutyl]-3-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



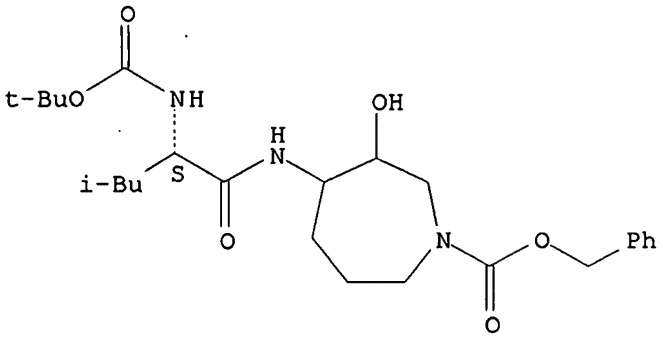
RN 339269-39-5 ZCAPLUS
CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[(4S)-hexahydro-2,4-d2-1-[(1-oxido-2-pyridinyl)sulfonyl]-3-oxo-1H-azepin-4-yl-2-d]amino]carbonyl]-3-methylbutyl]-3-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



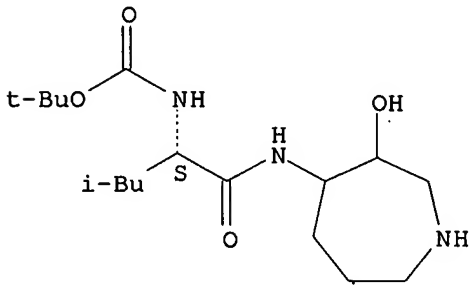
IT 281219-34-9P 281219-35-0P 281220-55-1P
281220-56-2P 281220-84-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of leucine aminoazepanone derivs. as protease inhibitors)
RN 281219-34-9 ZCAPLUS
CN 1H-Azepine-1-carboxylic acid, 4-[[(2S)-2-[[(1,1-dimethylethoxy)carbonyl]amino]-4-methyl-1-oxopentyl]amino]hexahydro-3-hydroxy-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



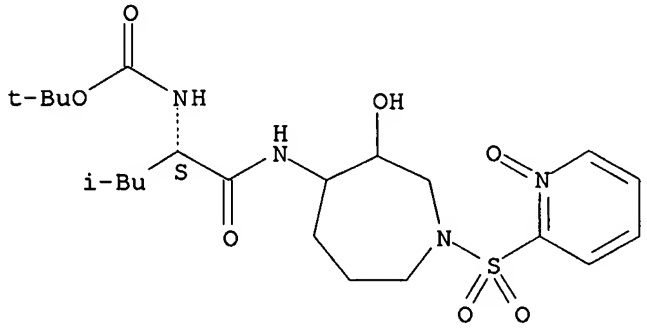
RN 281219-35-0 ZCAPLUS
CN Carbamic acid, [(1S)-1-[[(hexahydro-3-hydroxy-1H-azepin-4-yl)amino]carbonyl]-3-methylbutyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



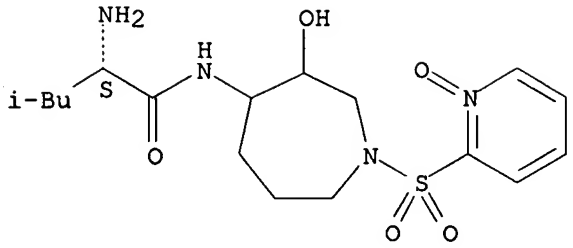
RN 281220-55-1 ZCAPLUS
CN Carbamic acid, [(1S)-1-[[[hexahydro-3-hydroxy-1-[(1-oxido-2-pyridinyl)sulfonyl]-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



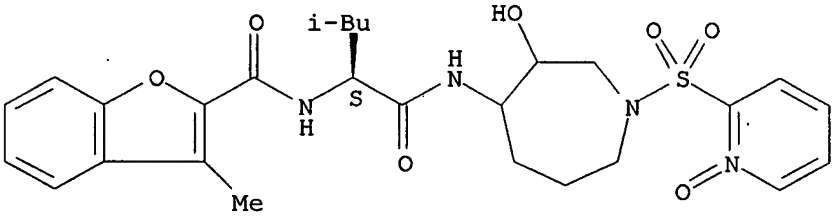
RN 281220-56-2 ZCAPLUS
CN Pentanamide, 2-amino-N-[hexahydro-3-hydroxy-1-[(1-oxido-2-pyridinyl)sulfonyl]-1H-azepin-4-yl]-4-methyl-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 281220-84-6 ZCAPLUS
CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[hexahydro-3-hydroxy-1-[(1-oxido-2-pyridinyl)sulfonyl]-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]-3-methyl- (9CI) (CA INDEX NAME)

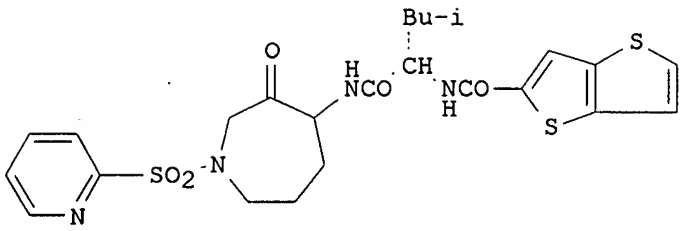
Absolute stereochemistry.



L4 ANSWER 49 OF 76 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:359960 ZCAPLUS
DOCUMENT NUMBER: 134:353549
TITLE: Preparation of leucine 4-aminoazepan-3-one derivatives as protease inhibitors
INVENTOR(S): Marquis, Robert W., Jr.; Ru, Yu; Veber, Daniel Frank
PATENT ASSIGNEE(S): SmithKline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001034565	A2	20010517	WO 2000-US30633	20001108
WO 2001034565	A3	20011004		
W: CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
EP 1235577	A2	20020904	EP 2000-975608	20001108
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR				
JP 2003513956	T	20030415	JP 2001-536514	20001108
PRIORITY APPLN. INFO.:			US 1999-164511P P	19991110
			WO 2000-US30633 W	20001108

GI



I

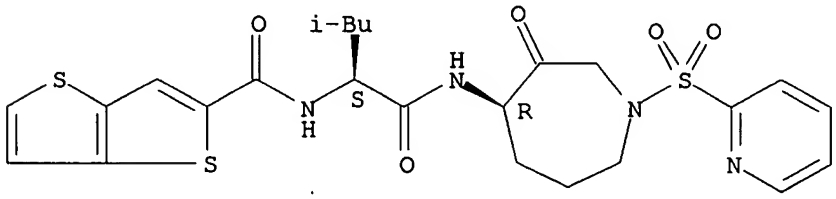
AB Thieno[3,2-b]thiophene-2-carboxylic acid amide I or a pharmaceutically acceptable salt, hydrate or solvate was prepared as an inhibitor of cysteine proteases, particularly cathepsin K, and is useful in the treatment of diseases in which inhibition of bone loss or of cartilage degradation is a factor. Thus, 4-amino-3-hydroxyazepane-1-carboxylic acid benzyl ester (preparation given) underwent sequential coupling with Boc-Leu-OH, catalytic hydrogenolysis, sulfonylation with 2-pyridinesulfonyl chloride, Boc-deprotection, acylation with thieno[3,2-b]thiophene-2-carboxylic acid, and hydroxyl group oxidation with pyridine-sulfur trioxide to afford I as a mixture of diastereomers which was separated by HPLC. I showed Ki = 0.09 nM and
pit assay = 50 nM in cathepsin K inhibition studies.

IT 281215-75-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of leucine aminoazepanone derivs. as protease inhibitors)

RN 281215-75-6 ZCAPLUS

CN Thieno[3,2-b]thiophene-2-carboxamide, N-[(1S)-1-[[[(4R)-hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

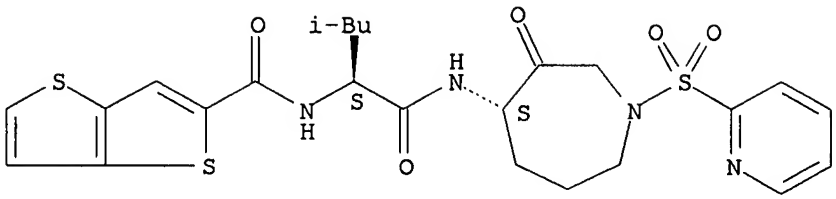


IT 281217-84-3P 281219-34-9P 281219-35-0P
281219-75-8P 281221-03-2P 339183-11-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of leucine aminoazepanone derivs. as protease inhibitors)

RN 281217-84-3 ZCAPLUS

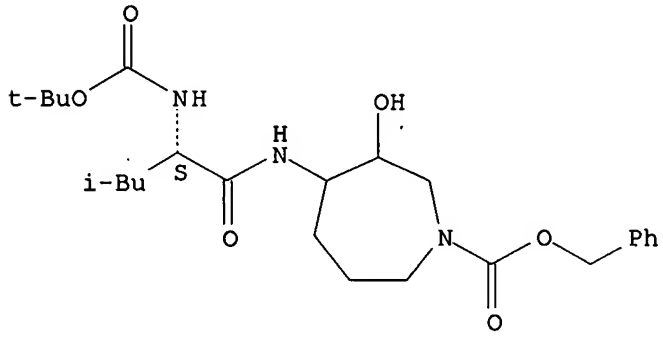
CN Thieno[3,2-b]thiophene-2-carboxamide, N-[(1S)-1-[[[(4S)-hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



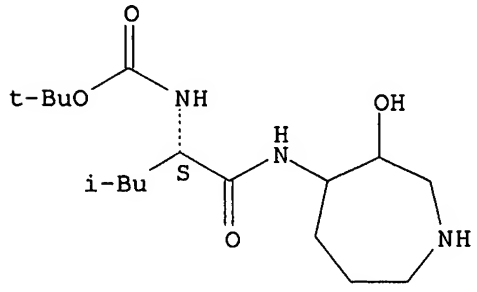
RN 281219-34-9 ZCAPLUS
CN 1H-Azepine-1-carboxylic acid, 4-[[(2S)-2-[[(1,1-dimethylethoxy)carbonyl]amino]-4-methyl-1-oxopentyl]amino]hexahydro-3-hydroxy-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



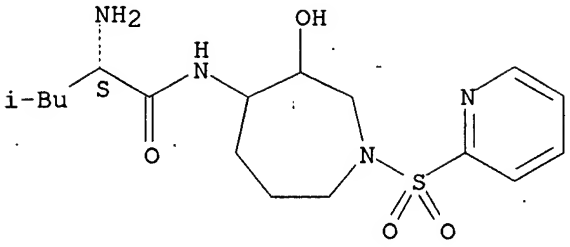
RN 281219-35-0 ZCAPLUS
CN Carbamic acid, [(1S)-1-[[(hexahydro-3-hydroxy-1H-azepin-4-yl)amino]carbonyl]-3-methylbutyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



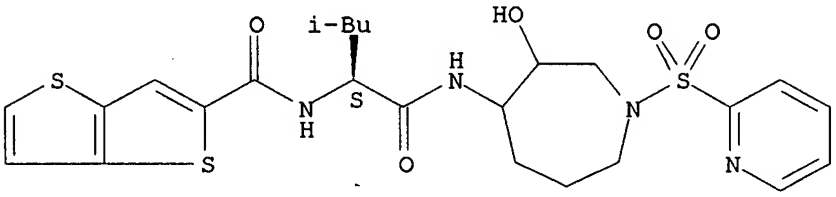
RN 281219-75-8 ZCAPLUS
CN Pentanamide, 2-amino-N-[hexahydro-3-hydroxy-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-4-methyl-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



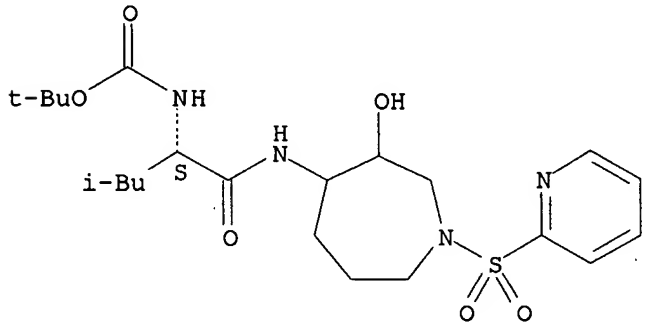
RN 281221-03-2 ZCAPLUS
CN Thieno[3,2-b]thiophene-2-carboxamide, N-[(1S)-1-[[[hexahydro-3-hydroxy-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 339183-11-8 ZCAPLUS
CN Carbamic acid, [(1S)-1-[[[hexahydro-3-hydroxy-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



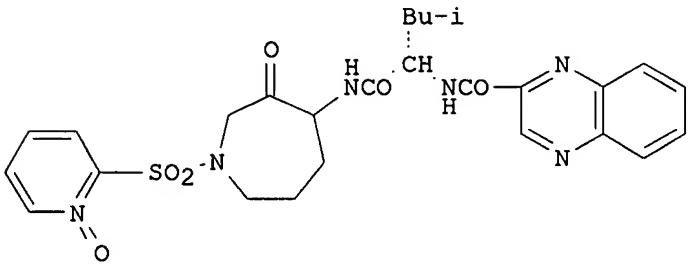
L4 ANSWER 50 OF 76 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:359809 ZCAPLUS
DOCUMENT NUMBER: 134:353548
TITLE: Preparation of leucine 4-aminoazepan-3-one derivatives as protease inhibitors
INVENTOR(S): Marquis, Robert W., Jr.; Ru, Yu; Veber, Daniel Frank
PATENT ASSIGNEE(S): SmithKline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

10/ 789,063

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001034160	A1	20010517	WO 2000-US30758	20001108
W: CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
EP 1229915	A1	20020814	EP 2000-978442	20001108
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR				
JP 2003513928	T	20030415	JP 2001-536158	20001108
PRIORITY APPLN. INFO.:			US 1999-164562P	P 19991110
			WO 2000-US30758	W 20001108

GI



I

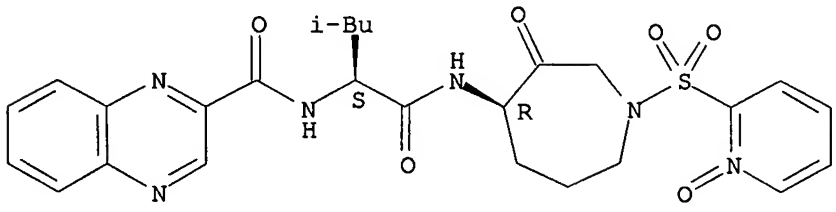
AB 2-Quinoxalinecarboxylic acid amide I or a pharmaceutically acceptable salt, hydrate or solvate was prepared as an inhibitor of cysteine proteases, particularly cathepsin K, and is useful in the treatment of diseases in which inhibition of bone loss or of cartilage degradation is a factor. Thus, 4-amino-3-hydroxyazepane-1-carboxylic acid benzyl ester (preparation given) underwent sequential coupling with Boc-Leu-OH, catalytic hydrogenolysis, sulfonylation with 2-pyridinesulfonyl chloride N-oxide, Boc-deprotection, acylation with 2-quinoxalinecarboxylic acid, and hydroxyl group oxidation with pyridine-sulfur trioxide to afford I as a mixture of diastereomers which was separated by HPLC. I showed Ki = 1.3 nM and pit assay ca. 100 nM in cathepsin K inhibition studies.

IT 281215-47-2P 281217-67-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of leucine aminoazepanone derivs. as protease inhibitors)

RN 281215-47-2 ZCAPLUS

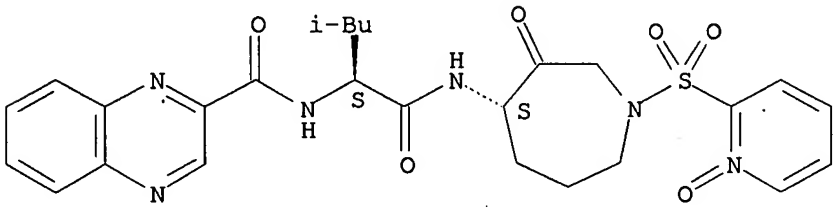
CN 2-Quinoxalinecarboxamide, N-[(1S)-1-[[[(4R)-hexahydro-1-[(1-oxido-2-pyridinyl)sulfonyl]-3-oxo-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



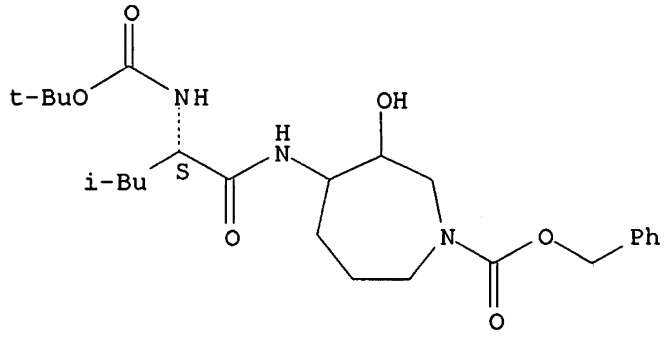
RN 281217-67-2 ZCAPLUS
CN 2-Quinoxalinecarboxamide, N-[(1S)-1-[[[(4S)-hexahydro-1-[(1-oxido-2-pyridinyl)sulfonyl]-3-oxo-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



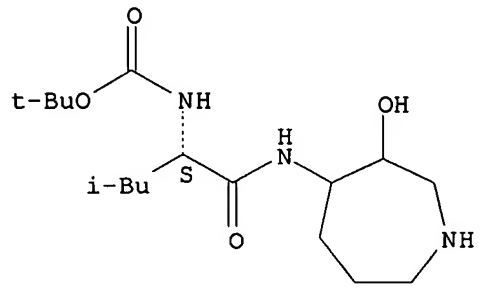
IT 281219-34-9P 281219-35-0P 281220-55-1P
281220-56-2P 281220-74-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of leucine aminoazepanone derivs. as protease inhibitors)
RN 281219-34-9 ZCAPLUS
CN 1H-Azepine-1-carboxylic acid, 4-[[(2S)-2-[[(1,1-dimethylethoxy)carbonyl]amino]-4-methyl-1-oxopentyl]amino]hexahydro-3-hydroxy-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



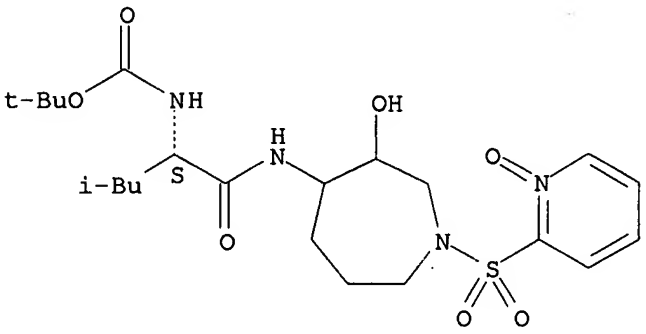
RN 281219-35-0 ZCAPLUS
CN Carbamic acid, [(1S)-1-[[(hexahydro-3-hydroxy-1H-azepin-4-yl)amino]carbonyl]-3-methylbutyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



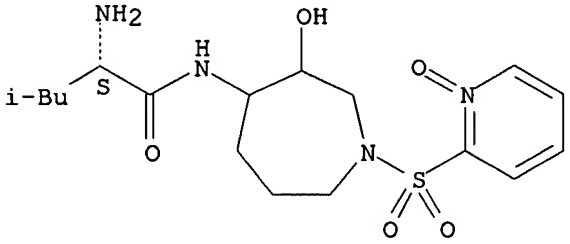
RN 281220-55-1 ZCAPLUS
CN Carbamic acid, [(1S)-1-[[[hexahydro-3-hydroxy-1-[(1-oxido-2-pyridinyl)sulfonyl]-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



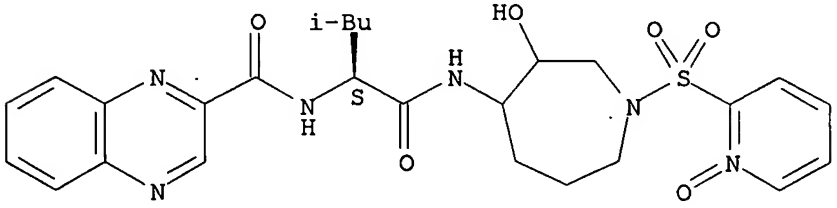
RN 281220-56-2 ZCAPLUS
CN Pentanamide, 2-amino-N-[hexahydro-3-hydroxy-1-[(1-oxido-2-pyridinyl)sulfonyl]-1H-azepin-4-yl]-4-methyl-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 281220-74-4 ZCAPLUS
CN 2-Quinoxalinecarboxamide, N-[(1S)-1-[[[hexahydro-3-hydroxy-1-[(1-oxido-2-pyridinyl)sulfonyl]-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



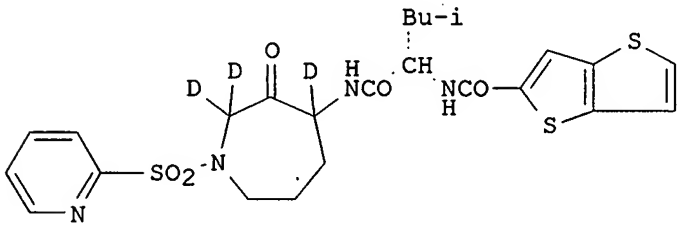
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 51 OF 76 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:359808 ZCAPLUS
DOCUMENT NUMBER: 134:353547
TITLE: Preparation of leucine 4-aminoazepan-3-one derivatives

as protease inhibitors
INVENTOR(S): Marquis, Robert Wells, Jr.; Veber, Daniel Frank
PATENT ASSIGNEE(S): SmithKline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001034159	A1	20010517	WO 2000-US30704	20001108
W: CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
EP 1231922	A1	20020821	EP 2000-977066	20001108
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR				
JP 2003513927	T	20030415	JP 2001-536157	20001108
PRIORITY APPLN. INFO.:			US 1999-164801P P	19991110
			WO 2000-US30704 W	20001108

GI



I

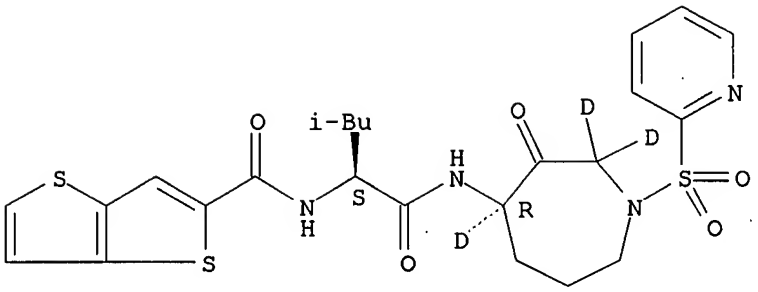
AB Thieno[3,2-b]thiophene-2-carboxylic acid amide I or a pharmaceutically acceptable salt, hydrate or solvate was prepared as an inhibitor of cysteine proteases, particularly cathepsin K, and is useful in the treatment of diseases in which inhibition of bone loss or of cartilage degradation is a factor. Thus, 4-amino-3-hydroxyazepane-1-carboxylic acid benzyl ester (preparation given) underwent sequential coupling with Boc-Leu-OH, catalytic hydrogenolysis, sulfonylation with 2-pyridinesulfonyl chloride, Boc-deprotection, acylation with thieno[3,2-b]thiophene-2-carboxylic acid, hydroxyl group oxidation with pyridine-sulfur trioxide, and deuteration to afford I as a mixture of diastereomers which was separated by HPLC.

IT 339195-31-2P 339195-32-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of leucine aminoazepanone derivs. as protease inhibitors)

RN 339195-31-2 ZCAPLUS

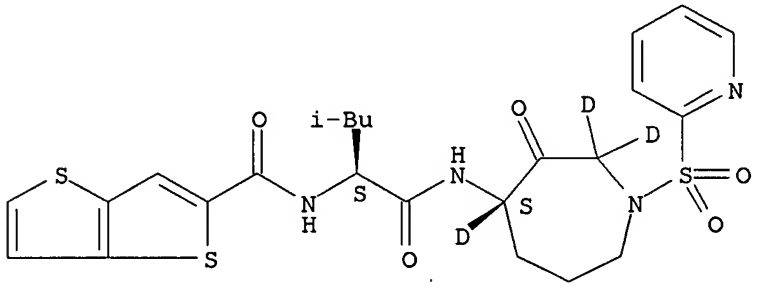
CN Thieno[3,2-b]thiophene-2-carboxamide, N-[(1S)-1-[[[(4R)-hexahydro-2,4-d2-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl-2-d]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



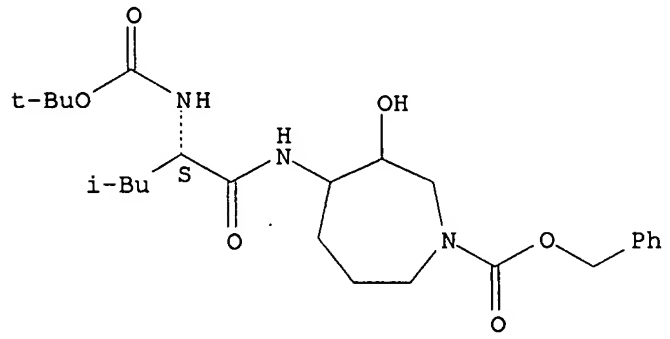
RN 339195-32-3 ZCAPLUS
CN Thieno[3,2-b]thiophene-2-carboxamide, N-[(1S)-1-[[[(4S)-hexahydro-2,4-d2-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl-2-d]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 281219-34-9P 281219-35-0P 281219-75-8P
281221-03-2P 339183-11-8P 339195-30-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of leucine aminoazepanone derivs. as protease inhibitors)
RN 281219-34-9 ZCAPLUS
CN 1H-Azepine-1-carboxylic acid, 4-[[(2S)-2-[[(1,1-dimethylethoxy)carbonyl]amino]-4-methyl-1-oxopentyl]amino]hexahydro-3-hydroxy-, phenylmethyl ester (9CI) (CA INDEX NAME)

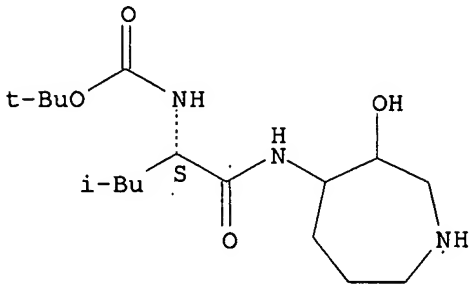
Absolute stereochemistry.



RN 281219-35-0 ZCAPLUS
CN Carbamic acid, [(1S)-1-[[(hexahydro-3-hydroxy-1H-azepin-4-yl)amino]carbonyl]-3-methylbutyl]-, 1,1-dimethylethyl ester (9CI) (CA

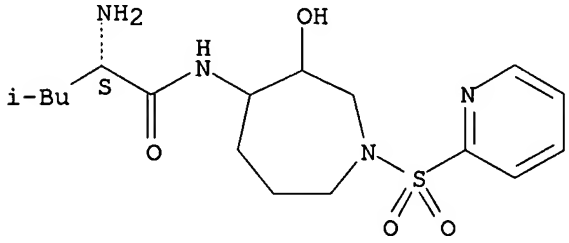
INDEX NAME)

Absolute stereochemistry.



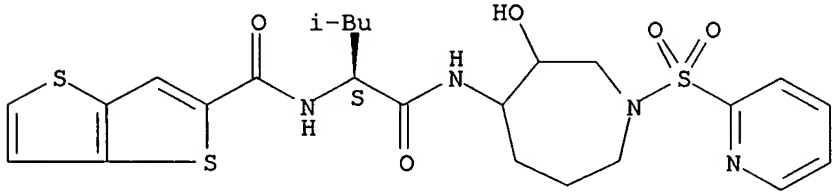
RN 281219-75-8 ZCAPLUS
CN Pentanamide, 2-amino-N-[hexahydro-3-hydroxy-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-4-methyl-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



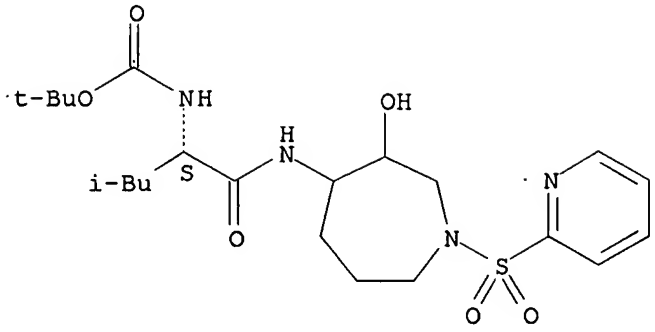
RN 281221-03-2 ZCAPLUS
CN Thieno[3,2-b]thiophene-2-carboxamide, N-[(1S)-1-[[[hexahydro-3-hydroxy-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



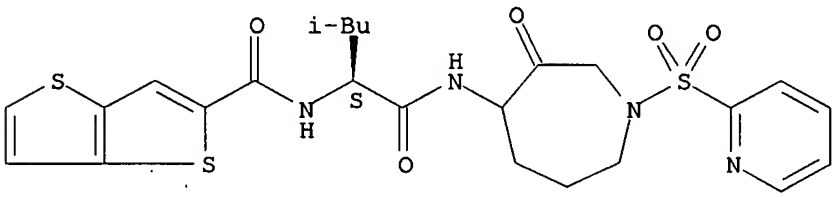
RN 339183-11-8 ZCAPLUS
CN Carbamic acid, [(1S)-1-[[[hexahydro-3-hydroxy-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 339195-30-1 ZCAPLUS
CN Thieno[3,2-b]thiophene-2-carboxamide, N-[(1S)-1-[[[hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

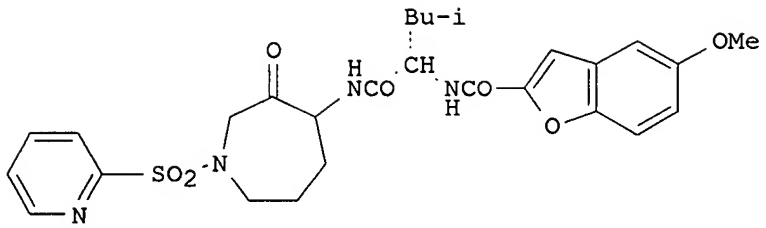


REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 52 OF 76 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:359807 ZCAPLUS
DOCUMENT NUMBER: 134:353546
TITLE: Preparation of leucine 4-aminoazepan-3-one derivatives as protease inhibitors
INVENTOR(S): Marquis, Robert W., Jr.; Ru, Yu; Veber, Daniel Frank
PATENT ASSIGNEE(S): SmithKline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2001034158	A1	20010517	WO 2000-US30703		20001108
W: CA, JP, US					
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR					
EP 1231921	A1	20020821	EP 2000-977065		20001108
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR					
JP 2003513926	T	20030415	JP 2001-536156		20001108
PRIORITY APPLN. INFO.:			US 1999-164576P	P	19991110
			WO 2000-US30703	W	20001108

GI



I

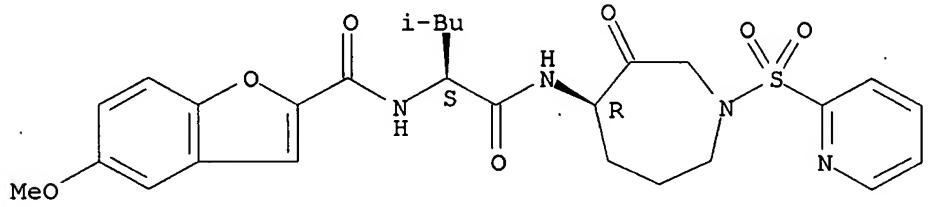
AB 5-Methoxybenzofuran-2-carboxylic acid amide I or a pharmaceutically acceptable salt, hydrate or solvate was prepared as an inhibitor of cysteine proteases, particularly cathepsin K, and is useful in the treatment of diseases in which inhibition of bone loss or of cartilage degradation is a factor. Thus, 4-amino-3-hydroxyazepane-1-carboxylic acid benzyl ester (preparation given) underwent sequential coupling with Boc-Leu-OH, catalytic hydrogenolysis, sulfonylation with 2-pyridinesulfonyl chloride, Boc-deprotection, acylation with 5-methoxybenzofuran-2-carboxylic acid, and hydroxyl group oxidation with pyridine-sulfur trioxide to afford I as a mixture of diastereomers which was separated by HPLC. I showed Ki = 0.4 nM and pit assay = 75 nM in cathepsin K inhibition studies.

IT 281215-11-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of leucine aminoazepanone derivs. as protease inhibitors)

RN 281215-11-0 ZCAPLUS

CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[(4R)-hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]-5-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

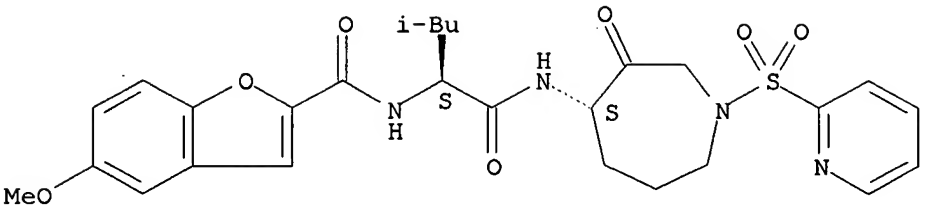


IT 281217-54-7P 281219-34-9P 281219-35-0P
281219-75-8P 281220-28-8P 339183-11-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of leucine aminoazepanone derivs. as protease inhibitors)

RN 281217-54-7 ZCAPLUS

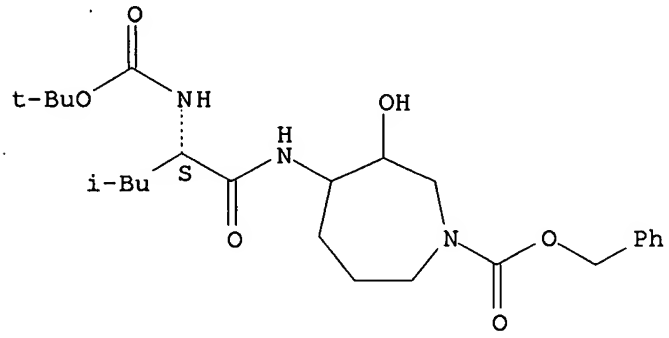
CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[(4S)-hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]-5-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



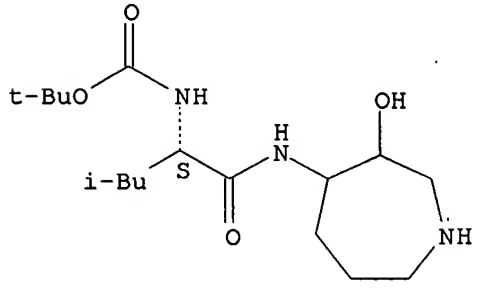
RN 281219-34-9 ZCAPLUS
CN 1H-Azepine-1-carboxylic acid, 4-[[(2S)-2-[[(1,1-dimethylethoxy)carbonyl]amino]-4-methyl-1-oxopentyl]amino]hexahydro-3-hydroxy-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



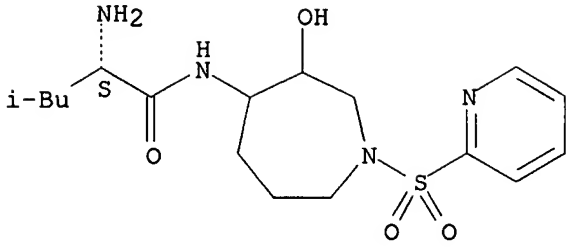
RN 281219-35-0 ZCAPLUS
CN Carbamic acid, [(1S)-1-[[(hexahydro-3-hydroxy-1H-azepin-4-yl)amino]carbonyl]-3-methylbutyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



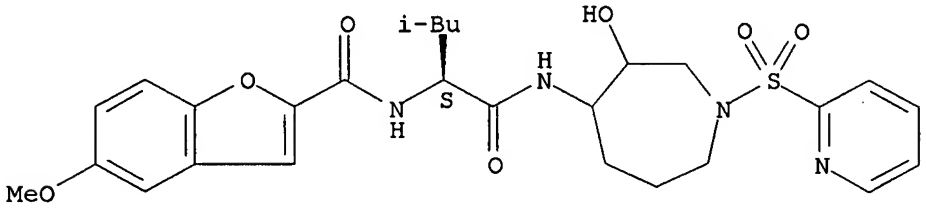
RN 281219-75-8 ZCAPLUS
CN Pentanamide, 2-amino-N-[hexahydro-3-hydroxy-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-4-methyl-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



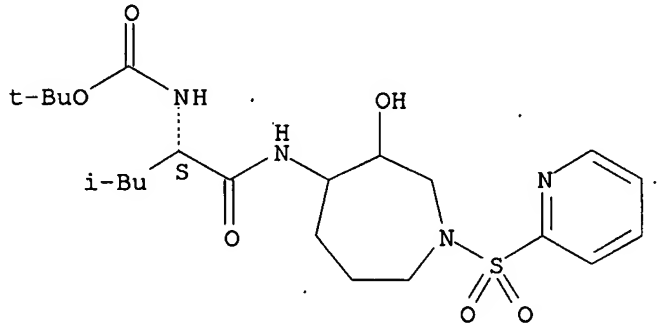
RN 281220-28-8 ZCAPLUS
CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[hexahydro-3-hydroxy-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]-5-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 339183-11-8 ZCAPLUS
CN Carbamic acid, [(1S)-1-[[[hexahydro-3-hydroxy-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



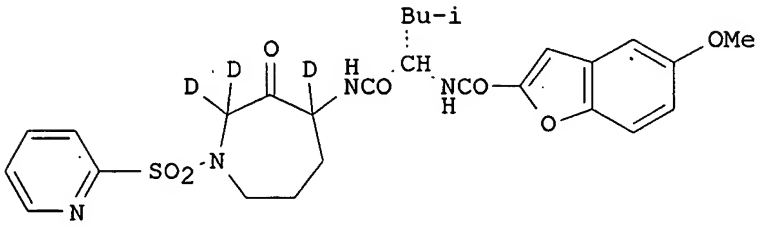
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 53 OF 76 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:359806 ZCAPLUS
DOCUMENT NUMBER: 134:353545
TITLE: Preparation of leucine 4-aminoazepan-3-one derivatives as protease inhibitors
INVENTOR(S): Marquis, Robert Wells, Jr.; Veber, Daniel Frank
PATENT ASSIGNEE(S): SmithKline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001034157	A1	20010517	WO 2000-US30702	20001108
W: CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
EP 1231923	A1	20020821	EP 2000-983690	20001108
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR				
JP 2003513925	T	20030415	JP 2001-536155	20001108
PRIORITY APPLN. INFO.:			US 1999-164577P P	19991110
			WO 2000-US30702 W	20001108

GI



I

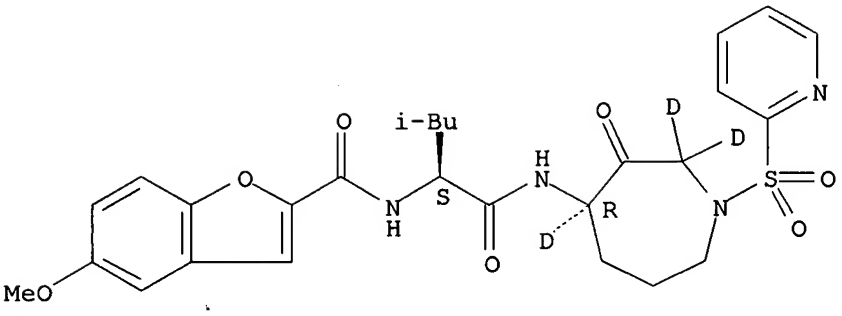
AB 5-Methoxybenzofuran-2-carboxylic acid amide I or a pharmaceutically acceptable salt, hydrate or solvate was prepared as an inhibitor of cysteine proteases, particularly cathepsin K, and is useful in the treatment of diseases in which inhibition of bone loss or of cartilage degradation is a factor. Thus, 4-amino-3-hydroxyazepane-1-carboxylic acid benzyl ester (preparation given) underwent sequential coupling with Boc-Leu-OH, catalytic hydrogenolysis, sulfonylation with 2-pyridinesulfonyl chloride, Boc-deprotection, acylation with 5-methoxybenzofuran-2-carboxylic acid, hydroxyl group oxidation with pyridine-sulfur trioxide, and deuteration to afford I as a mixture of diastereomers which was separated by HPLC.

IT 339183-13-0P 339183-14-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of leucine aminoazepanone derivs. as protease inhibitors)

RN 339183-13-0 ZCAPLUS

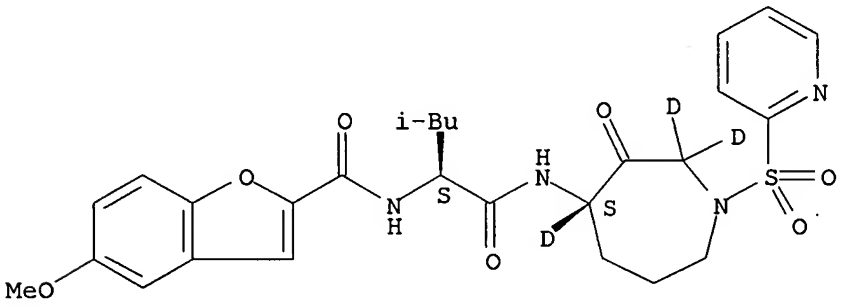
CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[(4R)-hexahydro-2,4-d2-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl-2-d]amino]carbonyl]-3-methylbutyl]-5-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



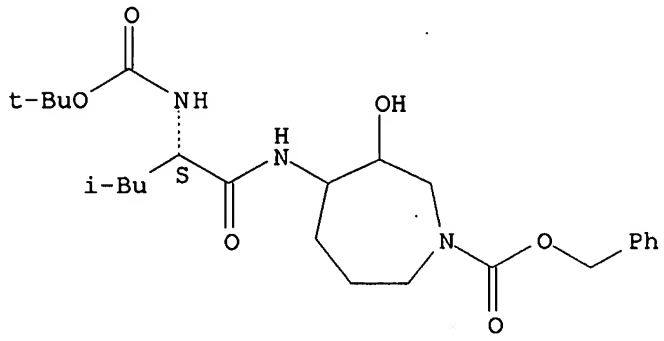
RN 339183-14-1 ZCAPLUS
CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[(4S)-hexahydro-2,4-d2-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl-2-d]amino]carbonyl]-3-methylbutyl]-5-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 281219-34-9P 281219-35-0P 281219-75-8P
281220-28-8P 339183-11-8P 339183-12-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of leucine aminoazepanone derivs. as protease inhibitors)
RN 281219-34-9 ZCAPLUS
CN 1H-Azepine-1-carboxylic acid, 4-[[(2S)-2-[[(1,1-dimethylethoxy)carbonyl]amino]-4-methyl-1-oxopentyl]amino]hexahydro-3-hydroxy-, phenylmethyl ester (9CI) (CA INDEX NAME)

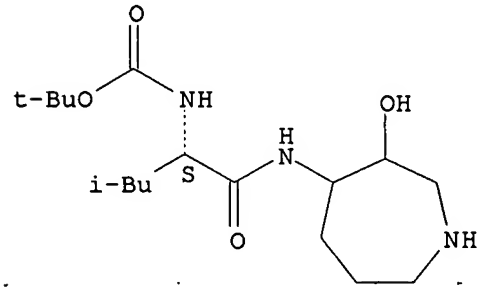
Absolute stereochemistry.



RN 281219-35-0 ZCAPLUS

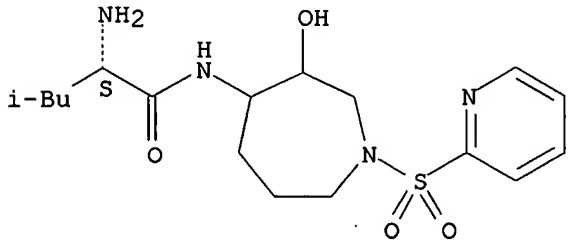
CN Carbamic acid, [(1S)-1-[[(hexahydro-3-hydroxy-1H-azepin-4-yl)amino]carbonyl]-3-methylbutyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



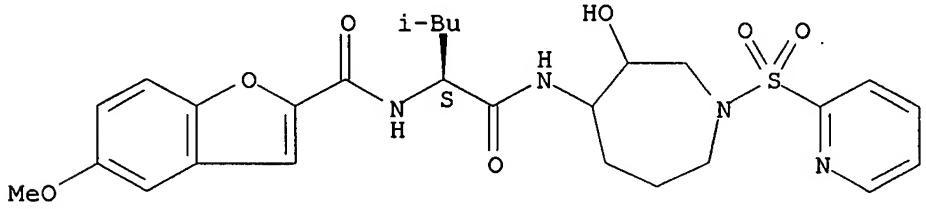
RN 281219-75-8 ZCAPLUS
CN Pentanamide, 2-amino-N-[hexahydro-3-hydroxy-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-4-methyl-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



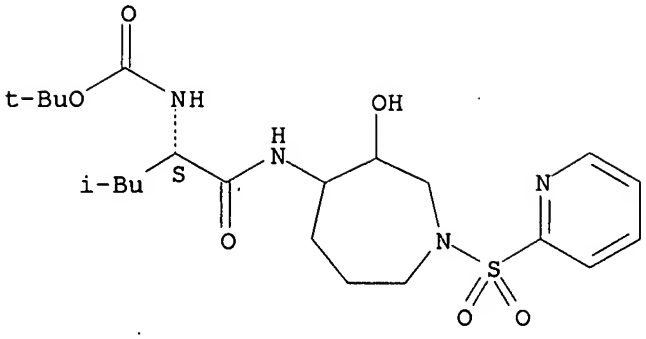
RN 281220-28-8 ZCAPLUS
CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[hexahydro-3-hydroxy-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]-5-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



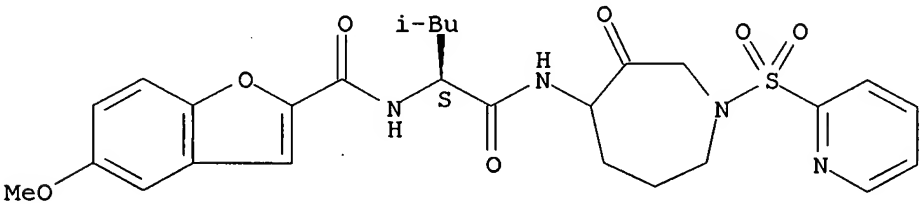
RN 339183-11-8 ZCAPLUS
CN Carbamic acid, [(1S)-1-[[[hexahydro-3-hydroxy-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 339183-12-9 ZCAPLUS
CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]-5-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

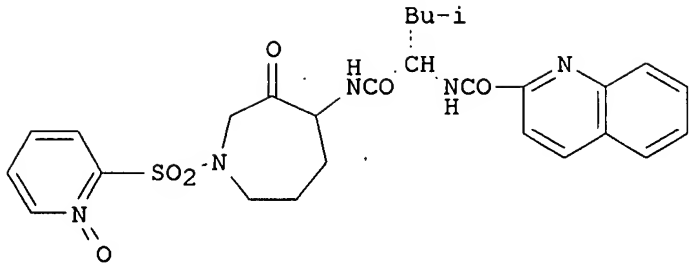


REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 54 OF 76 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:359805 ZCAPLUS
DOCUMENT NUMBER: 134:353544
TITLE: Preparation of leucine 4-aminoazepan-3-one derivatives as protease inhibitors
INVENTOR(S): Marquis, Robert W., Jr.; Ru, Yu; Veber, Daniel Frank
PATENT ASSIGNEE(S): SmithKline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001034156	A1	20010517	WO 2000-US30684	20001108
W: AU, CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
EP 1229914	A1	20020814	EP 2000-977057	20001108
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR				
JP 2003513924	T	20030415	JP 2001-536154	20001108
PRIORITY APPLN. INFO.:			US 1999-164578P P	19991110
			WO 2000-US30684 W	20001108

GI



I

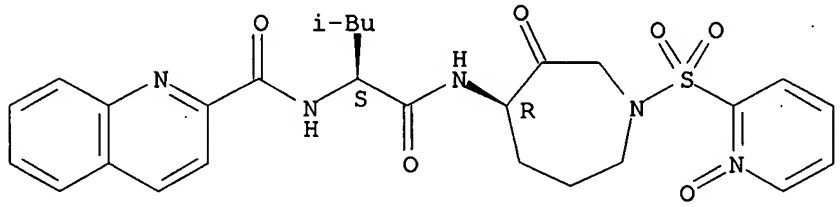
AB 2-Quinolinecarboxylic acid amide I or a pharmaceutically acceptable salt, hydrate or solvate was prepared as an inhibitor of cysteine proteases, particularly cathepsin K, and is useful in the treatment of diseases in which inhibition of bone loss or of cartilage degradation is a factor. Thus, 4-amino-3-hydroxyazepane-1-carboxylic acid benzyl ester (preparation given) underwent sequential coupling with Boc-Leu-OH, catalytic hydrogenolysis, sulfonylation with 2-pyridinesulfonyl chloride N-oxide, Boc-deprotection, acylation with 2-quinolinecarboxylic acid, and hydroxyl group oxidation with pyridine-sulfur trioxide to afford I as a mixture of diastereomers which was separated by HPLC. I showed Ki = 0.41 nM and pit assay = 300 nM in cathepsin K inhibition studies.

IT 281215-48-3P 281217-68-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of leucine aminoazepanone derivs. as protease inhibitors)

RN 281215-48-3 ZCAPLUS

CN 2-Quinolinecarboxamide, N-[(1S)-1-[[[(4R)-hexahydro-1-[(1-oxido-2-pyridinyl)sulfonyl]-3-oxo-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]-(9CI) (CA INDEX NAME)

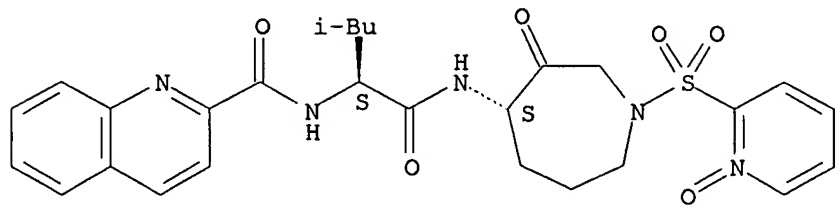
Absolute stereochemistry.



RN 281217-68-3 ZCAPLUS

CN 2-Quinolinecarboxamide, N-[(1S)-1-[[[(4S)-hexahydro-1-[(1-oxido-2-pyridinyl)sulfonyl]-3-oxo-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]-(9CI) (CA INDEX NAME)

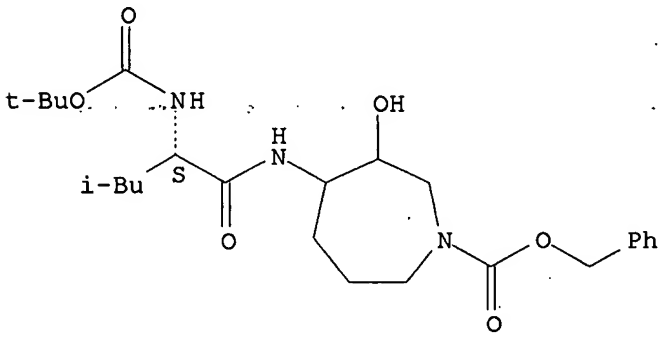
Absolute stereochemistry.



IT 281219-34-9P 281219-35-0P 281220-55-1P
281220-56-2P 281220-75-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of leucine aminoazepanone derivs. as protease inhibitors)

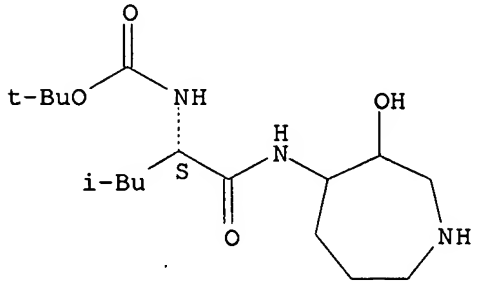
RN 281219-34-9 ZCAPLUS
CN 1H-Azepine-1-carboxylic acid, 4-[[(2S)-2-[[(1,1-dimethylethoxy)carbonyl]amino]-4-methyl-1-oxopentyl]amino]hexahydro-3-hydroxy-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



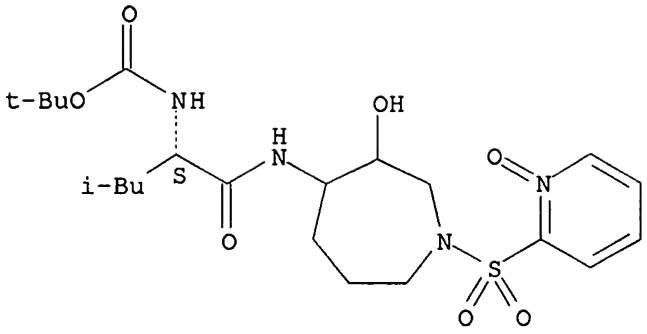
RN 281219-35-0 ZCAPLUS
CN Carbamic acid, [(1S)-1-[[(hexahydro-3-hydroxy-1H-azepin-4-yl)amino]carbonyl]-3-methylbutyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



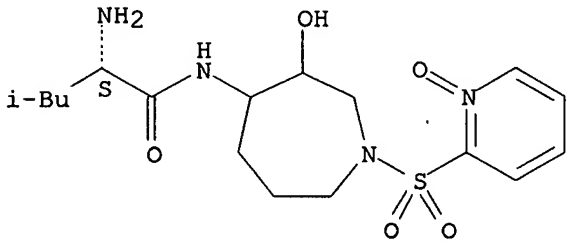
RN 281220-55-1 ZCAPLUS
CN Carbamic acid, [(1S)-1-[[[hexahydro-3-hydroxy-1-[(1-oxido-2-pyridinyl)sulfonyl]-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



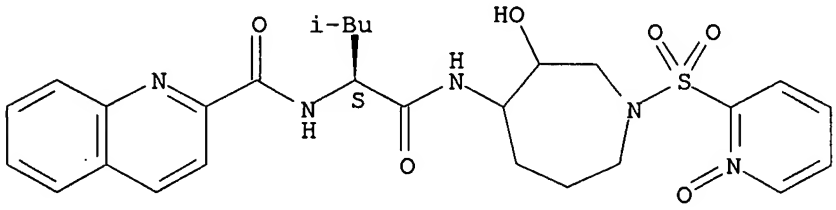
RN 281220-56-2 ZCAPLUS
CN Pentanamide, 2-amino-N-[hexahydro-3-hydroxy-1-[(1-oxido-2-pyridinyl)sulfonyl]-1H-azepin-4-yl]-4-methyl-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 281220-75-5 ZCAPLUS
CN 2-Quinolinecarboxamide, N-[(1S)-1-[[[hexahydro-3-hydroxy-1-[(1-oxido-2-pyridinyl)sulfonyl]-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

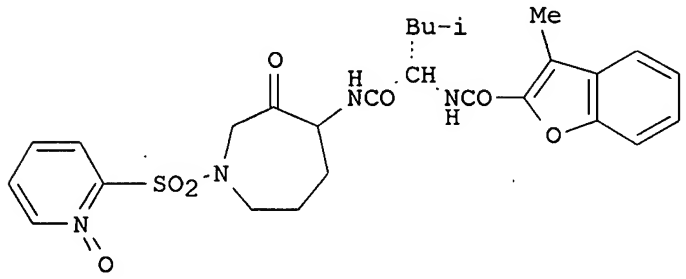
L4 ANSWER 55 OF 76 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:359804 ZCAPLUS
DOCUMENT NUMBER: 134:353543
TITLE: Preparation of leucine 4-aminoazepan-3-one derivatives as protease inhibitors
INVENTOR(S): Marquis, Robert W., Jr.; Ru, Yu; Veber, Daniel Frank
PATENT ASSIGNEE(S): SmithKline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

10/ 789,063

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001034155	A1	20010517	WO 2000-US30681	20001108
W: AU, CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
EP 1233771	A1	20020828	EP 2000-977055	20001108
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR				
JP 2003513923	T	20030415	JP 2001-536153	20001108
PRIORITY APPLN. INFO.:			US 1999-164800P P	19991110
			WO 2000-US30681 W	20001108

GI



I

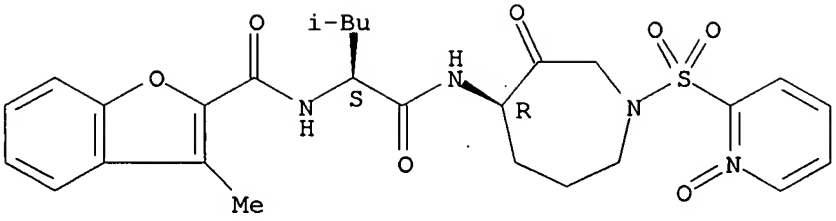
AB 3-Methylbenzofuran-2-carboxylic acid amide I or a pharmaceutically acceptable salt, hydrate or solvate was prepared as an inhibitor of cysteine proteases, particularly cathepsin K, and is useful in the treatment of diseases in which inhibition of bone loss or of cartilage degradation is a factor. Thus, 4-amino-3-hydroxyazepane-1-carboxylic acid benzyl ester (preparation given) underwent sequential coupling with Boc-Leu-OH, catalytic hydrogenolysis, sulfonylation with 2-pyridinesulfonyl chloride N-oxide, Boc-deprotection, acylation with 3-methylbenzofuran-2-carboxylic acid, and hydroxyl group oxidation with pyridine-sulfur trioxide to afford I as a mixture of diastereomers which was separated by HPLC. I showed Ki = 0.11 nM and pit assay = 40 nM in cathepsin K inhibition studies.

IT 281215-58-5P 281217-76-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of leucine aminoazepanone derivs. as protease inhibitors)

RN 281215-58-5 ZCAPLUS

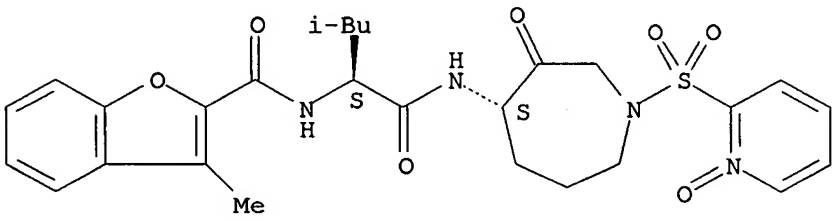
CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[(4R)-hexahydro-1-[(1-oxido-2-pyridinyl)sulfonyl]-3-oxo-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]-3-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



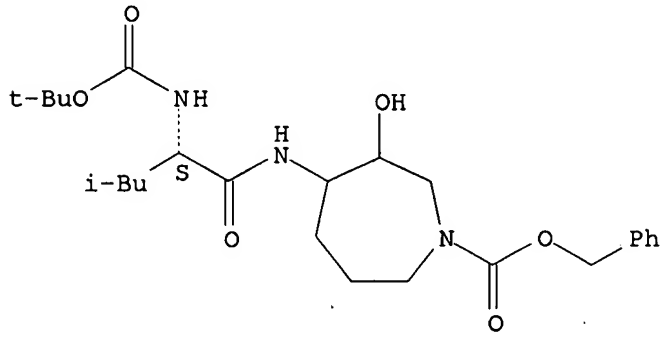
RN 281217-76-3 ZCAPLUS
CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[(4S)-hexahydro-1-[(1-oxido-2-pyridinyl)sulfonyl]-3-oxo-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]-3-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



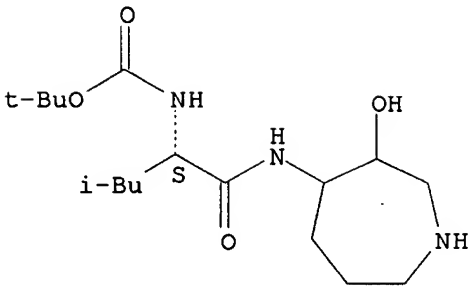
IT 281219-34-9P 281219-35-0P 281220-55-1P
281220-56-2P 281220-84-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of leucine aminoazepanone derivs. as protease inhibitors)
RN 281219-34-9 ZCAPLUS
CN 1H-Azepine-1-carboxylic acid, 4-[[(2S)-2-[[(1,1-dimethylethoxy)carbonyl]amino]-4-methyl-1-oxopentyl]amino]hexahydro-3-hydroxy-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



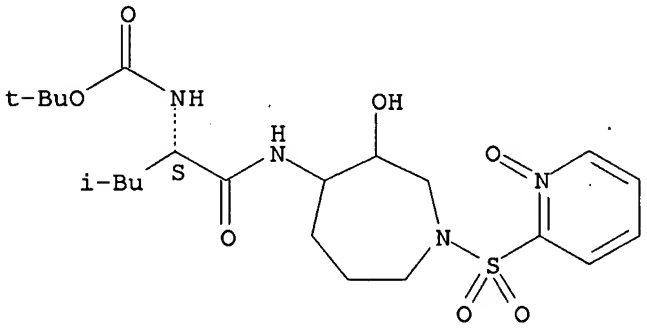
RN 281219-35-0 ZCAPLUS
CN Carbamic acid, [(1S)-1-[[(hexahydro-3-hydroxy-1H-azepin-4-yl)amino]carbonyl]-3-methylbutyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



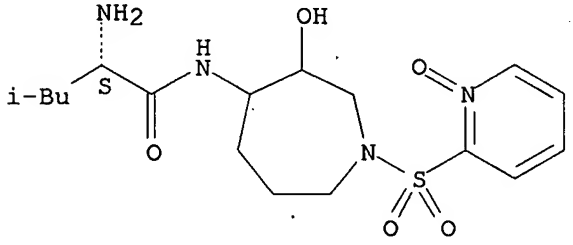
RN 281220-55-1 ZCAPLUS
CN Carbamic acid, [(1S)-1-[[[hexahydro-3-hydroxy-1-[(1-oxido-2-pyridinyl)sulfonyl]-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



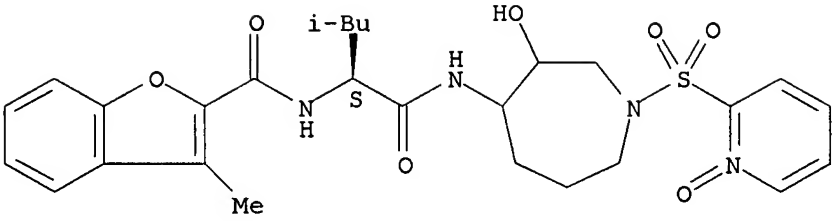
RN 281220-56-2 ZCAPLUS
CN Pentanamide, 2-amino-N-[hexahydro-3-hydroxy-1-[(1-oxido-2-pyridinyl)sulfonyl]-1H-azepin-4-yl]-4-methyl-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 281220-84-6 ZCAPLUS
CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[hexahydro-3-hydroxy-1-[(1-oxido-2-pyridinyl)sulfonyl]-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]-3-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

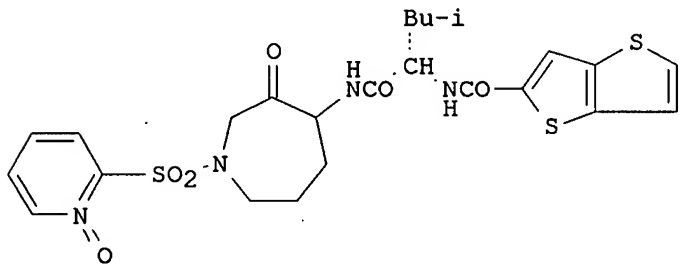


REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 56 OF 76 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:359803 ZCAPLUS
DOCUMENT NUMBER: 134:353542
TITLE: Preparation of leucine 4-aminoazepan-3-one derivatives as protease inhibitors
INVENTOR(S): Marquis, Robert W., Jr.; Ru, Yu; Veber, Daniel Frank
PATENT ASSIGNEE(S): SmithKline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001034154	A1	20010517	WO 2000-US30634	20001108
W: CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
EP 1229912	A1	20020814	EP 2000-975609	20001108
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR				
JP 2003513922	T	20030415	JP 2001-536152	20001108
PRIORITY APPLN. INFO.:			US 1999-164559P P	19991110
			WO 2000-US30634 W	20001108

GI



I

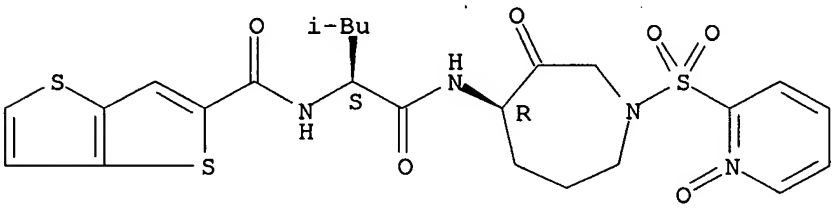
AB Thieno[3,2-b]thiophene-2-carboxylic acid amide I or a pharmaceutically acceptable salt, hydrate or solvate was prepared as an inhibitor of cysteine proteases, particularly cathepsin K, and is useful in the treatment of diseases in which inhibition of bone loss or of cartilage degradation is a factor. Thus, 4-amino-3-hydroxyazepane-1-carboxylic acid benzyl ester (preparation given) underwent sequential coupling with Boc-Leu-OH, catalytic

hydrogenolysis, sulfonylation with 2-pyridinesulfonyl chloride N-oxide, Boc-deprotection, acylation with thieno[3,2-b]thiophene-2-carboxylic acid, and hydroxyl group oxidation with pyridine-sulfur trioxide to afford I as a mixture of diastereomers which was separated by HPLC. I showed Ki = 0.14 nM and
pit assay = 45 nM in cathepsin K inhibition studies.

IT 281215-46-1P 281217-66-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of leucine aminoazepanone derivs. as protease inhibitors)

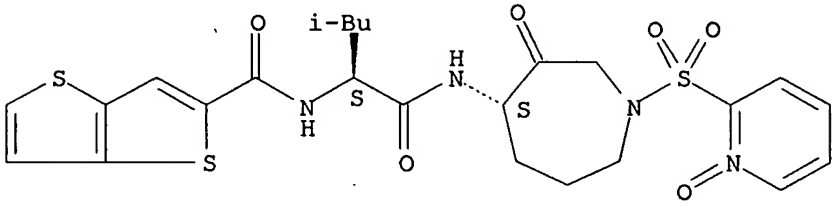
RN 281215-46-1 ZCAPLUS
CN Thieno[3,2-b]thiophene-2-carboxamide, N-[(1S)-1-[[[(4R)-hexahydro-1-[(1-oxido-2-pyridinyl)sulfonyl]-3-oxo-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 281217-66-1 ZCAPLUS
CN Thieno[3,2-b]thiophene-2-carboxamide, N-[(1S)-1-[[[(4S)-hexahydro-1-[(1-oxido-2-pyridinyl)sulfonyl]-3-oxo-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

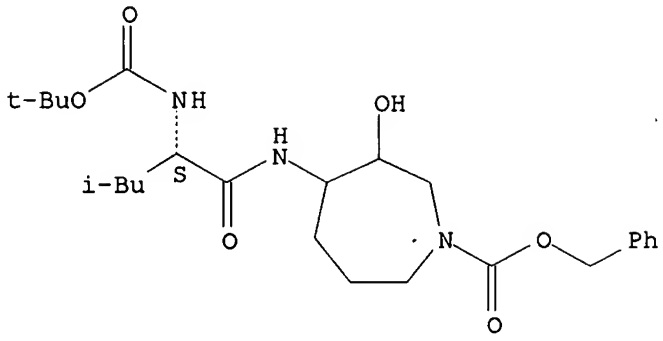
Absolute stereochemistry.



IT 281219-34-9P 281219-35-0P 281220-55-1P
281220-56-2P 281220-73-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of leucine aminoazepanone derivs. as protease inhibitors)

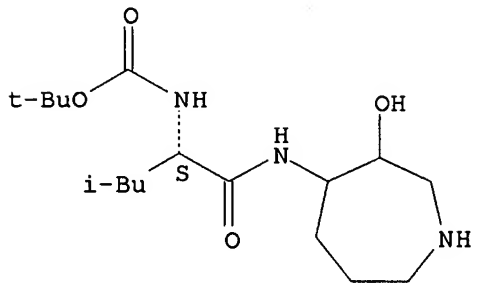
RN 281219-34-9 ZCAPLUS
CN 1H-Azepine-1-carboxylic acid, 4-[[(2S)-2-[[(1,1-dimethylethoxy)carbonyl]amino]-4-methyl-1-oxopentyl]amino]hexahydro-3-hydroxy-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



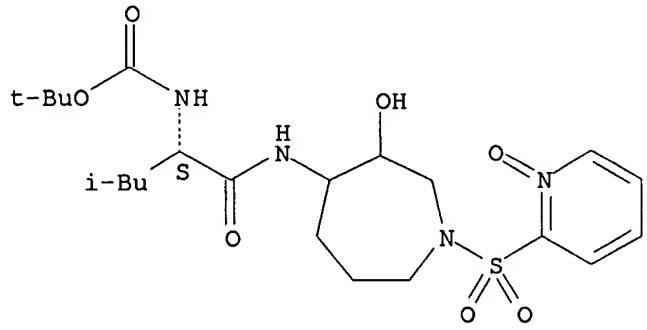
RN 281219-35-0 ZCAPLUS
CN Carbamic acid, [(1S)-1-[[(hexahydro-3-hydroxy-1H-azepin-4-yl)amino]carbonyl]-3-methylbutyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



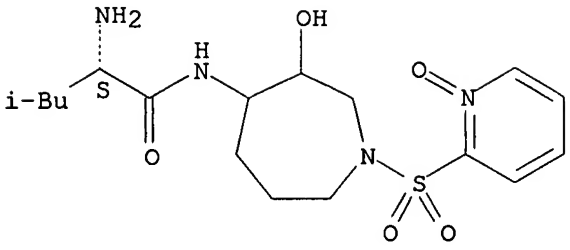
RN 281220-55-1 ZCAPLUS
CN Carbamic acid, [(1S)-1-[[[hexahydro-3-hydroxy-1-[(1-oxido-2-pyridinyl)sulfonyl]-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



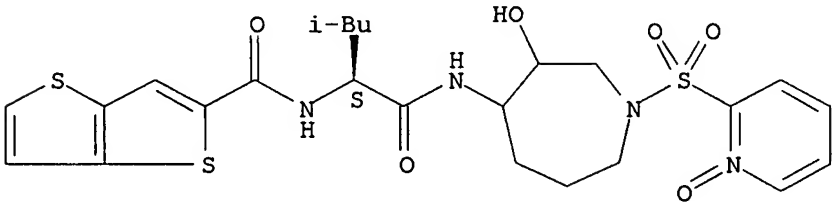
RN 281220-56-2 ZCAPLUS
CN Pentanamide, 2-amino-N-[hexahydro-3-hydroxy-1-[(1-oxido-2-pyridinyl)sulfonyl]-1H-azepin-4-yl]-4-methyl-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 281220-73-3 ZCAPLUS
CN Thieno[3,2-b]thiophene-2-carboxamide, N-[(1S)-1-[[[hexahydro-3-hydroxy-1-[(1-oxido-2-pyridinyl)sulfonyl]-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 57 OF 76 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:359802 ZCAPLUS
DOCUMENT NUMBER: 134:353541
TITLE: Preparation of leucine 4-aminoazepan-3-one derivatives as protease inhibitors
INVENTOR(S): Marquis, Robert Wells, Jr.; Veber, Daniel Frank
PATENT ASSIGNEE(S): SmithKline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2001034153	A1	20010517	WO 2000-US30632		20001108
W: CA, JP, US					
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR					
EP 1229911	A1	20020814	EP 2000-975607		20001108
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR					
JP 2003513921	T	20030415	JP 2001-536151		20001108
PRIORITY APPLN. INFO.:			US 1999-164515P	P	19991110
			WO 2000-US30632	W	20001108

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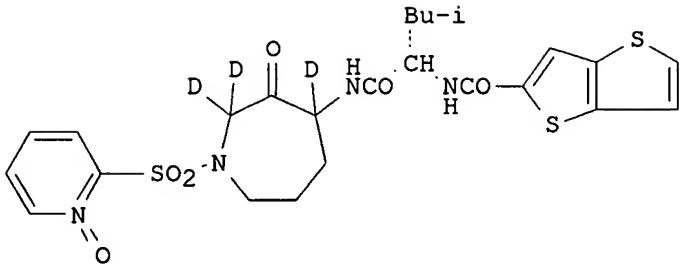


I

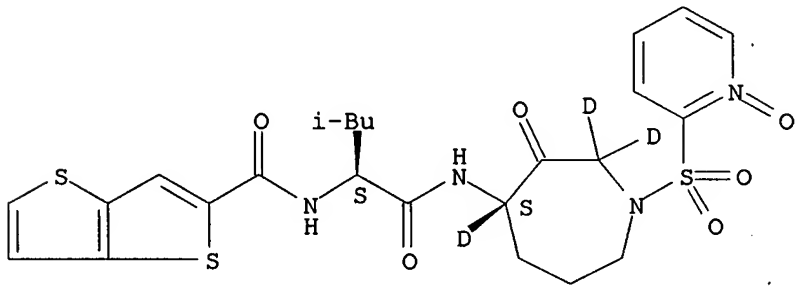
AB Thieno[3,2-b]thiophene-2-carboxylic acid amide I or a pharmaceutically acceptable salt, hydrate or solvate was prepared as an inhibitor of cysteine proteases, particularly cathepsin K, and is useful in the treatment of diseases in which inhibition of bone loss or of cartilage degradation is a factor. Thus, 4-amino-3-hydroxyazepane-1-carboxylic acid benzyl ester (preparation given) underwent sequential coupling with Boc-Leu-OH, catalytic hydrogenolysis, sulfonylation with 2-pyridinesulfonyl chloride N-oxide, Boc-deprotection, acylation with thieno[3,2-b]thiophene-2-carboxylic acid, hydroxyl group oxidation with pyridine-sulfur trioxide, and deuteration to afford I as a mixture of diastereomers which was separated by HPLC.

IT 339075-63-7P 339075-64-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of leucine aminoazepanone derivs. as protease inhibitors)

RN 339075-63-7 ZCAPLUS

CN Thieno[3,2-b]thiophene-2-carboxamide, N-[(1S)-1-[[[(4S)-hexahydro-2,4-d2-1-[(1-oxido-2-pyridinyl)sulfonyl]-3-oxo-1H-azepin-4-yl-2-d]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

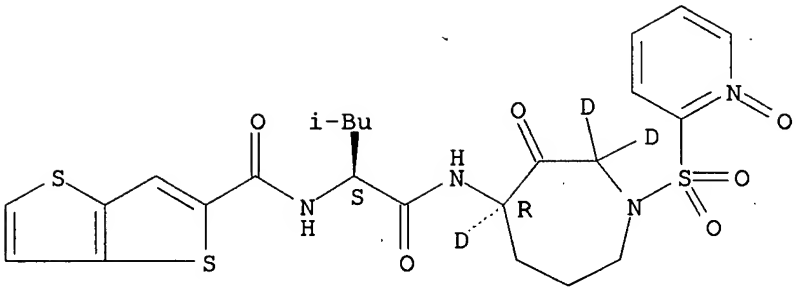
Absolute stereochemistry.



RN 339075-64-8 ZCAPLUS

CN Thieno[3,2-b]thiophene-2-carboxamide, N-[(1S)-1-[[[(4R)-hexahydro-2,4-d2-1-[(1-oxido-2-pyridinyl)sulfonyl]-3-oxo-1H-azepin-4-yl-2-d]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

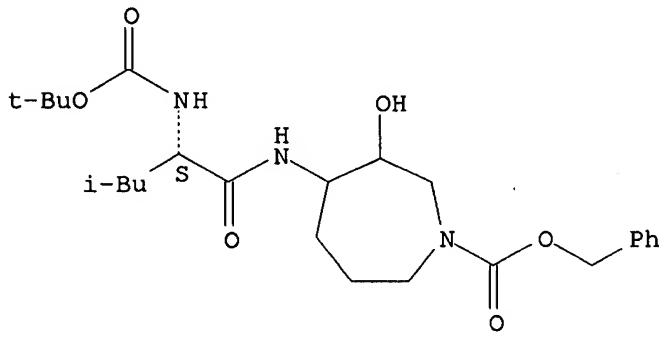


IT 281219-34-9P 281219-35-0P 281220-55-1P
281220-56-2P 281220-73-3P 339075-62-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of leucine aminoazepanone derivs. as protease inhibitors)

RN 281219-34-9 ZCAPLUS

CN 1H-Azepine-1-carboxylic acid, 4-[[(2S)-2-[[(1,1-dimethylethoxy)carbonyl]amino]-4-methyl-1-oxopentyl]amino]hexahydro-3-hydroxy-, phenylmethyl ester (9CI) (CA INDEX NAME)

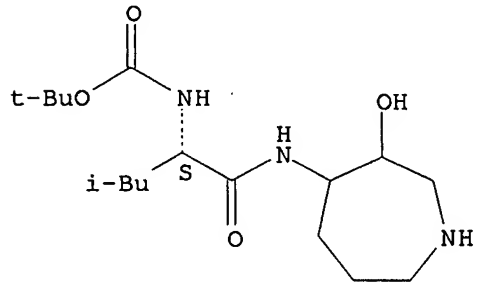
Absolute stereochemistry.



RN 281219-35-0 ZCAPLUS

CN Carbamic acid, [(1S)-1-[[(hexahydro-3-hydroxy-1H-azepin-4-yl)amino]carbonyl]-3-methylbutyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

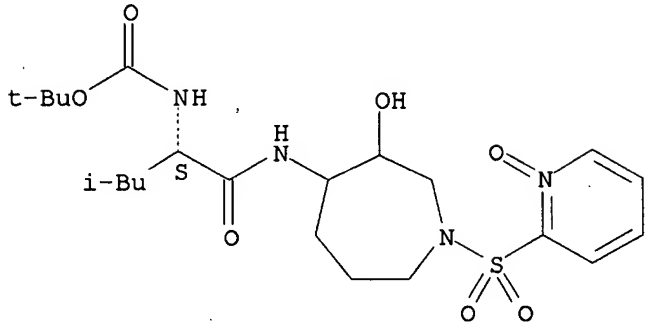


RN 281220-55-1 ZCAPLUS

CN Carbamic acid, [(1S)-1-[[[hexahydro-3-hydroxy-1-[(1-oxido-2-pyridinyl)sulfonyl]-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]-,

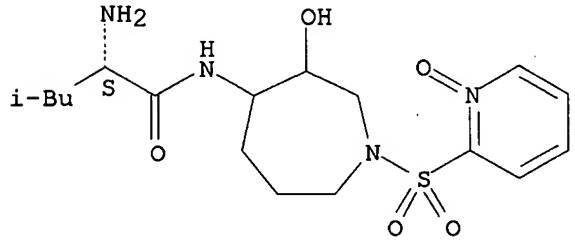
1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



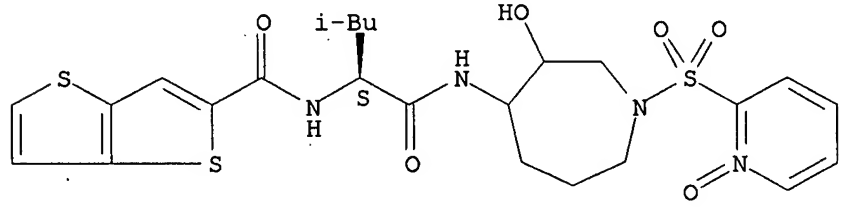
RN 281220-56-2 ZCAPLUS
CN Pentanamide, 2-amino-N-[hexahydro-3-hydroxy-1-[(1-oxido-2-pyridinyl)sulfonyl]-1H-azepin-4-yl]-4-methyl-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



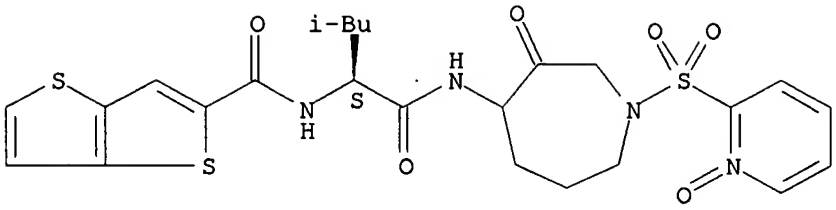
RN 281220-73-3 ZCAPLUS
CN Thieno[3,2-b]thiophene-2-carboxamide, N-[(1S)-1-[[[hexahydro-3-hydroxy-1-[(1-oxido-2-pyridinyl)sulfonyl]-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 339075-62-6 ZCAPLUS
CN Thieno[3,2-b]thiophene-2-carboxamide, N-[(1S)-1-[[[hexahydro-1-[(1-oxido-2-pyridinyl)sulfonyl]-3-oxo-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

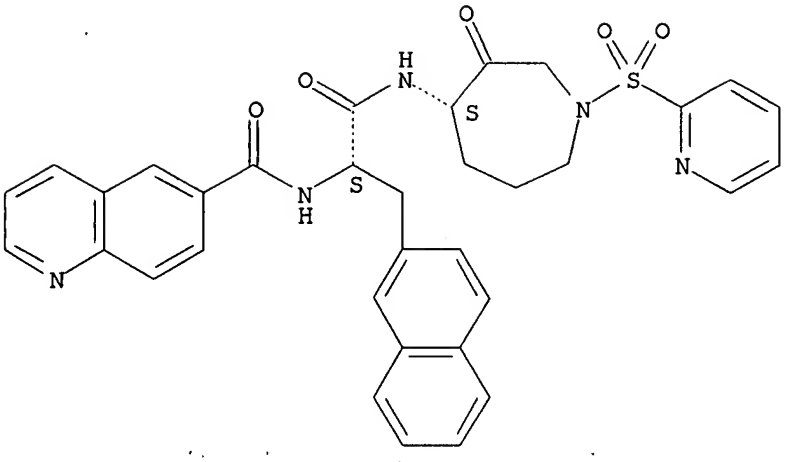
L4 ANSWER 58 OF 76 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:318582 ZCAPLUS
DOCUMENT NUMBER: 135:120165
TITLE: Potent and selective cathepsin L inhibitors do not inhibit human osteoclast resorption in vitro
AUTHOR(S): James, Ian E.; Marquis, Robert W.; Blake, Simon M.; Hwang, Shing Mei; Gress, Catherine J.; Ru, Yu; Zembryki, Denise; Yamashita, Dennis S.; McQueney, Michael S.; Tomaszek, Thaddeus A.; Oh, Hye-Ja; Gowen, Maxine; Veber, Daniel F.; Lark, Michael W.
CORPORATE SOURCE: Departments of Bone and Cartilage Biology, SmithKline Beecham Pharmaceuticals, King of Prussia, PA, 19406, USA
SOURCE: Journal of Biological Chemistry (2001), 276(15), 11507-11511
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Cathepsins K and L are related cysteine proteases that have been proposed to play important roles in osteoclast-mediated bone resorption. To further examine the putative role of cathepsin L in bone resorption, we have evaluated selective and potent inhibitors of human cathepsin L and cathepsin K in an in vitro assay of human osteoclastic resorption and an in situ assay of osteoclast cathepsin activity. The potent selective cathepsin L inhibitors (Ki = 0.0099, 0.034, and 0.27 nM) were inactive in both the in situ cytochem. assay (IC50 > 1 μM) and the osteoclast-mediated bone resorption assay (IC50 > 300 nM). Conversely, the cathepsin K selective inhibitor was potently active in both the cytochem. (IC50 = 63 nM) and resorption (IC50 = 71 nM) assays. A recently reported dipeptide aldehyde with activity against cathepsins L (Ki = 0.052 nM) and K (Ki = 1.57 nM) was also active in both assays (IC50 = 110 and 115 nM, resp.) These data confirm that cathepsin K and not cathepsin L is the major protease responsible for human osteoclastic bone resorption.

IT 350796-38-2 350796-39-3 350796-41-7
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(potent and selective cathepsin L inhibitors do not inhibit human osteoclast resorption in vitro)

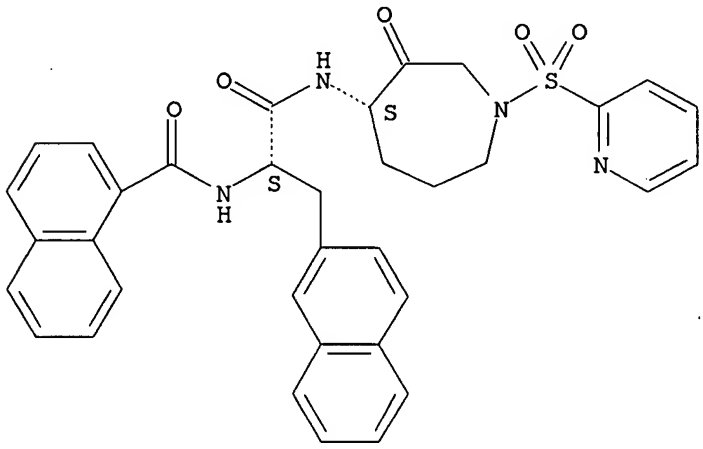
RN 350796-38-2 ZCAPLUS
CN 6-Quinolinecarboxamide, N-[(1S)-2-[[(4S)-hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]-1-(2-naphthalenylmethyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



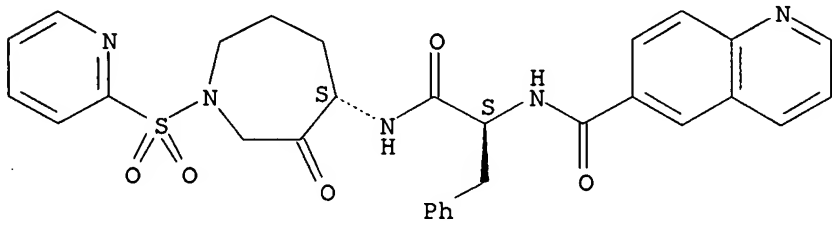
RN 350796-39-3 ZCAPLUS
CN 2-Naphthalenepropanamide, N-[(4S)-hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-α-[(1-naphthalenylcarbonyl)amino]-, (αS)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 350796-41-7 ZCAPLUS
CN 6-Quinolinecarboxamide, N-[(1S)-2-[[(4S)-hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]-2-oxo-1-(phenylmethyl)ethyl]-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 59 OF 76 ZCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:215566 ZCAPLUS
DOCUMENT NUMBER: 135:5780

TITLE: Azepanone-Based Inhibitors of Human and Rat Cathepsin K

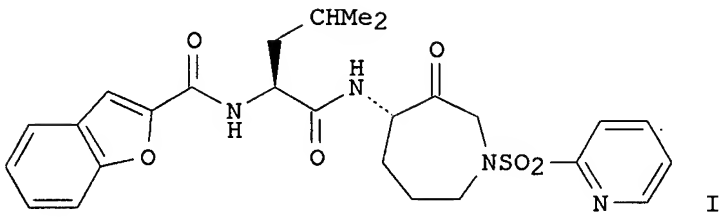
AUTHOR(S): Marquis, Robert W.; Ru, Yu; LoCastro, Steven M.; Zeng, Jin; Yamashita, Dennis S.; Oh, Hye-Ja; Erhard, Karl F.; Davis, Larry D.; Tomaszek, Thaddeus A.; Tew, David; Salyers, Kevin; Proksch, Joel; Ward, Keith; Smith, Brian; Levy, Mark; Cummings, Maxwell D.; Haltiwanger, R. Curtis; Trescher, Gudrun; Wang, Bing; Hemling, Mark E.; Quinn, Chad J.; Cheng, H-Y.; Lin, Fan; Smith, Ward W.; Janson, Cheryl A.; Zhao, Baoguang; McQueney, Michael S.; D'Alessio, Karla; Lee, Chao-Pin; Marzulli, Antonia; Dodds, Robert A.; Blake, Simon; Hwang, Shing-Mei; James, Ian E.; Gress, Catherine J.; Bradley, Brian R.; Lark, Michael W.; Gowen, Maxine; Veber, Daniel F.

CORPORATE SOURCE: Departments of Medicinal Chemistry Mechanistic Enzymology Drug Metabolism and Pharmacokinetics Physical and Structural Chemistry Structural Biology Protein Biochemistry Life-Cycle Management and Drug Delivery Systems and Bone and Cartilage Biology, GlaxoSmithKline, King of Prussia, PA, 19406, USA

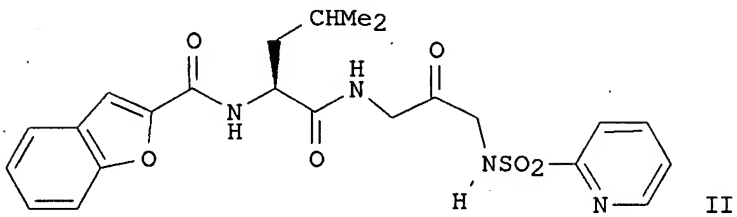
SOURCE: Journal of Medicinal Chemistry (2001), 44(9), 1380-1395
CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

GI



I



II

AB The synthesis, in vitro activities, and pharmacokinetics of a series of azepanone-based inhibitors of the cysteine protease cathepsin K (EC

3.4.22.38) are described. These compds. show improved configurational stability of the C-4 diastereomeric center relative to the previously published five- and six-membered ring ketone-based inhibitor series. Studies in this series have led to the identification of azepanone I, a potent, selective inhibitor of human cathepsin K (Ki = 0.16 nM) as well as the acyclic analog II, a potent inhibitor of both human (Ki = 0.0048 nM) and rat (Ki,app = 4.8 nM) cathepsin K. Small-mol. X-ray crystallog. anal. of I established the C-4 S stereochem. as being critical for potent inhibition and that unbound I adopted the expected equatorial conformation for the C-4 substituent. Mol. modeling studies predicted the higher energy axial orientation at C-4 of I when bound within the active site of cathepsin K, a feature subsequently confirmed by X-ray crystallog. Pharmacokinetic studies in the rat show I to be 42% orally bioavailable. Comparison of the transport of the cyclic and acyclic analogs through CaCo-2 cells suggests that oral bioavailability of the acyclic derivs. is limited by a P-glycoprotein-mediated efflux mechanism. It is concluded that the introduction of a conformational constraint has served the dual purpose of increasing inhibitor potency by locking in a bioactive conformation as well as locking out available conformations which may serve as substrates for enzyme systems that limit oral bioavailability.

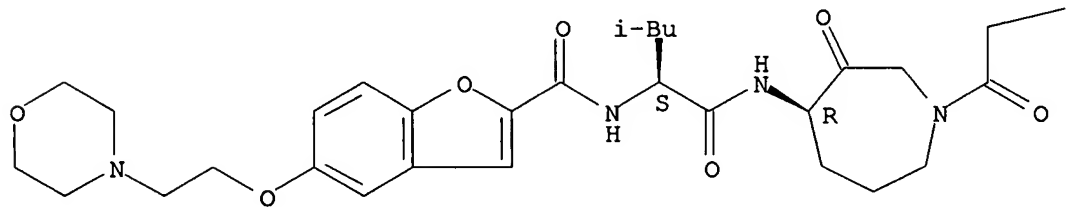
IT 281214-55-9P 281214-75-3P 281217-40-1P
281217-45-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process); RACT (Reactant or reagent)
(preparation of benzofurylcarbonylleucylazepinone cathepsin K inhibitors)

RN 281214-55-9 ZCAPLUS

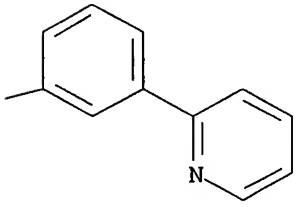
CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[(4R)-hexahydro-3-oxo-1-[[3-(2-pyridinyl)phenyl]acetyl]-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]-5-[2-(4-morpholinyl)ethoxy]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

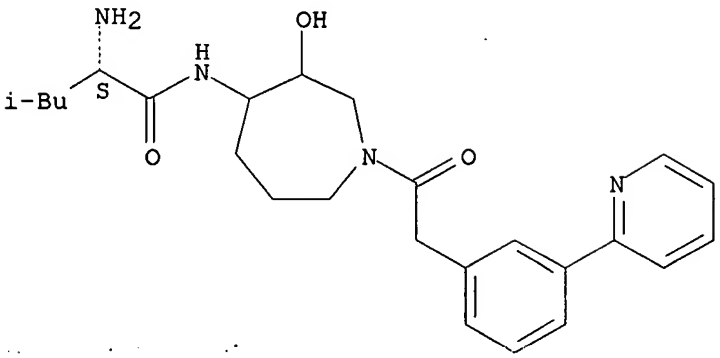


PAGE 1-B



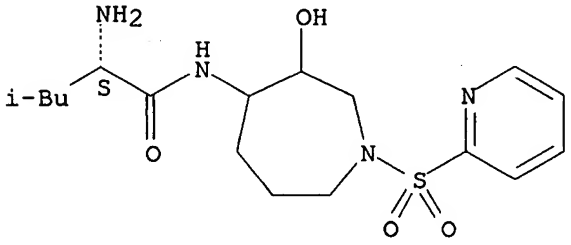
NAME)

Absolute stereochemistry.



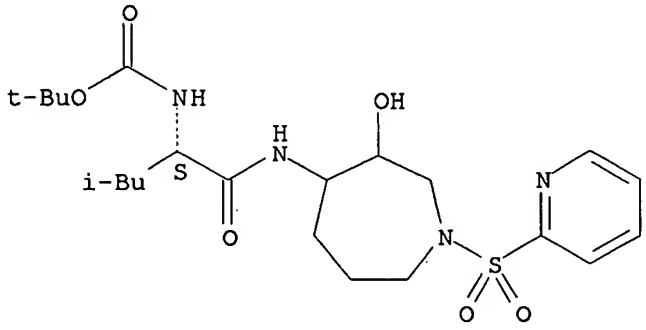
RN 281219-75-8 ZCAPLUS
CN Pentanamide, 2-amino-N-[hexahydro-3-hydroxy-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-4-methyl-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 339183-11-8 ZCAPLUS
CN Carbamic acid, [(1S)-1-[[[hexahydro-3-hydroxy-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 66 THERE ARE 66 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 60 OF 76 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:55540 ZCAPLUS
DOCUMENT NUMBER: 134:246869

10/ 789,063

TITLE: Cyclic Ketone Inhibitors of the Cysteine Protease Cathepsin K

AUTHOR(S): Marquis, Robert W.; Ru, Yu; Zeng, Jin; Trout, Robert E. Lee; LoCastro, Stephen M.; Gribble, Andrew D.; Witherington, Jason; Fenwick, Ashley E.; Garnier, Benedicte; Tomaszek, Thaddeus; Tew, David; Hemling, Mark E.; Quinn, Chad J.; Smith, Ward W.; Zhao, Baoguang; McQueney, Michael S.; Janson, Cheryl A.; D'Alessio, Karla; Veber, Daniel F.

CORPORATE SOURCE: Departments of Medicinal Chemistry (U.S.A.) Medicinal Chemistry (U.K.) Molecular Recognition Physical and Structural Chemistry Structural Biology and Protein Biochemistry GlaxoSmithKline, Harlow Essex, CM19 5AW, UK

SOURCE: Journal of Medicinal Chemistry (2001), 44(5), 725-736
CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 134:246869

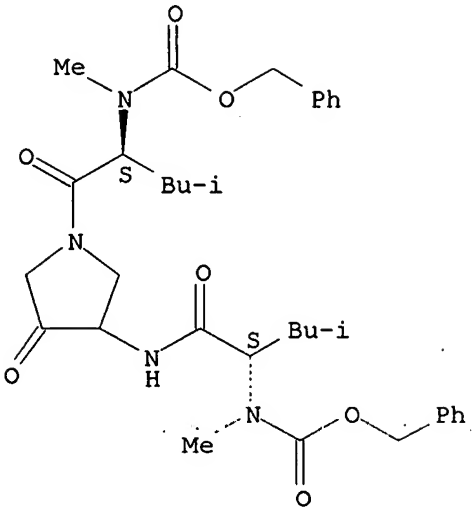
AB Cathepsin K (EC 3.4.22.38), a cysteine protease of the papain superfamily, is predominantly expressed in osteoclasts and has been postulated as a target for the treatment of osteoporosis. Crystallog. and structure-activity studies on a series of acyclic ketone-based inhibitors of cathepsin K have led to the design and identification of two series of cyclic ketone inhibitors. The mode of binding for four of these cyclic and acyclic inhibitors to cathepsin K is discussed and compared. All of the structures are consistent with addition of the active site thiol to the ketone of the inhibitors with the formation of a hemithioketal. Cocrystn. of the C-3 diastereomeric 3-amidotetrahydrofuran-4-one analog with cathepsin K showed the inhibitor to occupy the unprimed side of the active site with the 3S diastereomer preferred. This C-3 stereochem. preference is in contrast to the x-ray cocrystal structures of the 3-amidopyrrolidin-4-one inhibitors which show these inhibitors to prefer binding of the 3R diastereomer. The 3-amidopyrrolidin-4-one inhibitors were bound in the active site of the enzyme in two alternate directions. Epimerization issues associated with the labile α-amino ketone diastereomeric center contained within these inhibitor classes has proven to limit their utility despite promising pharmacokinetics displayed in both series of compds.

IT 203500-95-2 330975-08-1
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(cyclic ketone inhibitors of cysteine protease cathepsin K)

RN 203500-95-2 ZCAPLUS

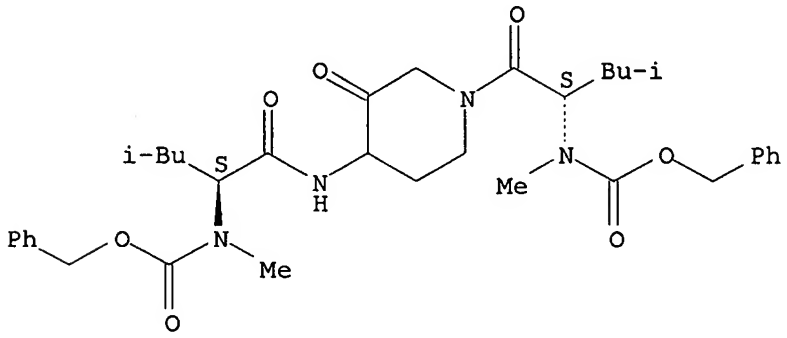
CN Carbamic acid, methyl[(1S)-3-methyl-1-[[3-[[(2S)-4-methyl-2-[methyl[(phenylmethoxy)carbonyl]amino]-1-oxopentyl]amino]-4-oxo-1-pyrrolidinyl]carbonyl]butyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 330975-08-1 ZCAPLUS
CN Carbamic acid, methyl[(1S)-3-methyl-1-[[4-[[(2S)-4-methyl-2-[methyl[(phenylmethoxy)carbonyl]amino]-1-oxopentyl]amino]-3-oxo-1-piperidinyl]carbonyl]butyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 330975-09-2 330975-10-5
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(cyclic ketone inhibitors of cysteine protease cathepsin K)
RN 330975-09-2 ZCAPLUS
CN Carbamic acid, methyl[(1S)-3-methyl-1-[[[1-[(2S)-4-methyl-2-(methylamino)-1-oxopentyl]-4-oxo-3-pyrrolidinyl]amino]carbonyl]butyl]-, phenylmethyl ester, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 61 OF 76 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:881147 ZCAPLUS
DOCUMENT NUMBER: 134:42137
TITLE: Preparation of pyrrolidinyl, piperidinyl or homopiperidinyl substituted benzodioxan, benzofuran or benzopyran derivatives for treating conditions which are related to impaired fundic relaxation
INVENTOR(S): De Bruyn, Marcel Frans Leopold; Van Emelen, Kristof; Wigerinck, Piet Tom Bert Paul; Verschueren, Wim Gaston
PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000075137	A1	20001214	WO 2000-EP4747	20000523
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2374905	A1	20001214	CA 2000-2374905	20000523
BR 2000011247	A	20020305	BR 2000-11247	20000523
EP 1187831	A1	20020320	EP 2000-927243	20000523
EP 1187831	B1	20041013		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
TR 200103433	T2	20020621	TR 2001-3433	20000523
HU 200201344	A2	20020828	HU 2002-1344	20000523
JP 2003501428	T	20030114	JP 2001-502420	20000523
EE 200100640	A	20030217	EE 2001-640	20000523
EE 4720	B1	20061016		
NZ 515478	A	20030328	NZ 2000-515478	20000523
CN 1131862	B	20031224	CN 2000-808317	20000523
AT 279409	T	20041015	AT 2000-927243	20000523
AU 777601	B2	20041021	AU 2000-45685	20000523
ES 2231189	T3	20050516	ES 2000-927243	20000523
US 6900222	B1	20050531	US 2001-980451	20000523
TW 575571	B	20040211	TW 2000-89109976	20000524
HR 2001000869	A1	20030831	HR 2001-869	20011122
BG 106157	A	20020628	BG 2001-106157	20011128
MX 2001PA12323	A	20020722	MX 2001-PA12323	20011129
ZA 2001009863	A	20030228	ZA 2001-9863	20011129
NO 2001005865	A	20020201	NO 2001-5865	20011130
US 2005159406	A1	20050721	US 2005-79606	20050314

PRIORITY APPLN. INFO.:
EP 1999-201746 A 19990602
WO 2000-EP4747 W 20000523
US 2001-980451 A3 20011130

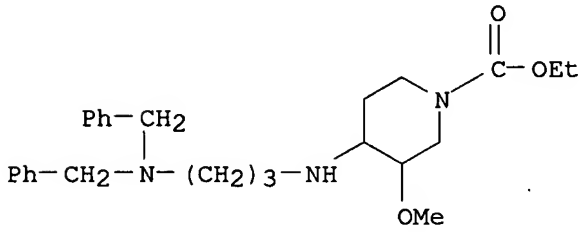
OTHER SOURCE(S): MARPAT 134:42137
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

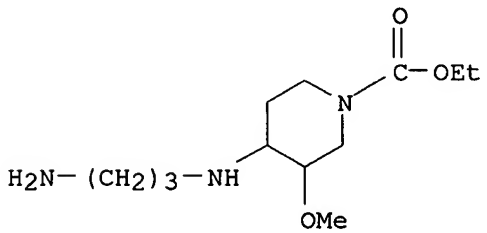
AB The title compds. [I; Alk = (un)substituted alkanediyl, alkylcarbonyl, carbonylalkyl, etc.; Z1Z2 = OCHR4CH2, OCHR4CH2O, OCHR4CH2S, etc.; R1-R3 = H, alkyl, OH, etc.; or when R1 and R2 are on adjacent carbon atoms, R1 and R2 taken together may form (CH2)3, OCH2CH2, (CH2)4, etc.; R4 = H, alkyl, hydroxyalkyl, etc.; the bivalent radical A = substituted piperidinyl, (un)substituted pyrrolidinyl, homopiperidinyl, etc.; R5 = II-IV, etc. (wherein X = O, S, NR9, CHNO2; Y = O, S; R7 = H, alkyl, cycloalkyl, etc.; R8 = alkyl, cycloalkyl, Ph, phenylmethyl; R9 = CN, alkyl, cycloalkyl, etc.; R10 = H, alkyl; Q = (CH2)2, (CH2)3, CH:CH, etc.)] and their pharmaceutically acceptable acid addition salts, useful as a medicine, in particular for treating conditions which are related to impaired fundic relaxation, were prepared E.g., a multi-step synthesis of the pyrimidinone (R)-V which showed the mean maximal change of 178 mL in volume on relaxation of the fundus, during the 1 h observation period after i.d. administration at 0.63 mg/kg, was given.

IT 312928-10-2P 312928-13-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of pyrrolidinyl, piperidinyl or homopiperidinyl substituted benzodioxan, benzofuran or benzopyran derivs. for treating conditions which are related to impaired fundic relaxation)

RN 312928-10-2 ZCAPLUS
CN 1-Piperidinecarboxylic acid, 4-[[3-[bis(phenylmethyl)amino]propyl]amino]-3-methoxy-, ethyl ester (9CI) (CA INDEX NAME)



RN 312928-13-5 ZCAPLUS
CN 1-Piperidinecarboxylic acid, 4-[(3-aminopropyl)amino]-3-methoxy-, ethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 62 OF 76 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:659781 ZCAPLUS
DOCUMENT NUMBER: 133:238331

10/ 789,063

TITLE: Preparation of selectively N-alkylated peptidomimetic compounds and combinatorial libraries
INVENTOR(S): Dorner, Barbara; Ostresh, John M.; Dooley, Colette T.; Houghten, Richard A.; Eichler, Jutta
PATENT ASSIGNEE(S): Trega Biosciences, Inc., USA
SOURCE: U.S., 26 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6121489	A	20000919	US 1997-811830	19970305
US 6143932	A	20001107	US 1999-346005	19990701
PRIORITY APPLN. INFO.:			US 1996-46871P P	19960305
			US 1997-811830 A1	19970305

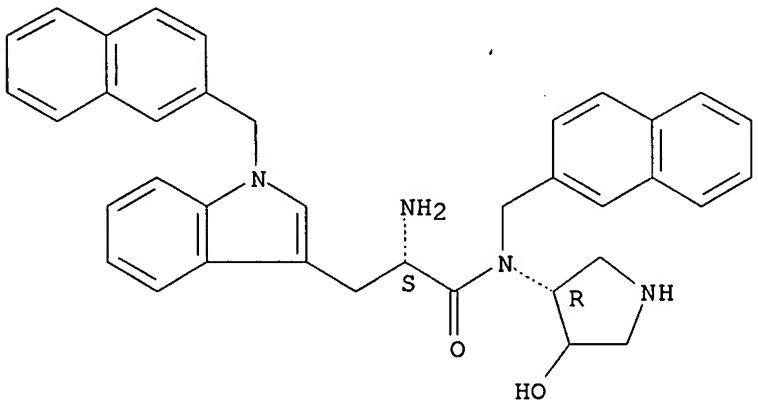
OTHER SOURCE(S): MARPAT 133:238331

AB Peptidomimetics R1R2R10NCHR3(CH2)m(CXY)[NR4CHR5(CH2)n(CXY)]qNR6CHR7(CH2)p(CXY)NR8R9 [I; R1, R2 = H, an amino protecting group, acyl, cycloalkyl, (un)substituted alkyl or alkylaryl; R3, R5, R7 = H, (un)substituted alkyl, Ph, or alkylaryl; R4, R6, R8 is a C1 to C18 substituent group, with that all but one can be the same group; R9 is H or a solid support; R10 is optionally present as a C1 to C18 substituent group when one of R1 and R2 is absent and the other is not H or an amino protecting group; m, n, p = 0-5; q = 0-3] were prepared as single compds. or as libraries. The invention is directed to methods of effecting analgesia, a decrease in the postprandial rise in the blood glucose levels of a mammal after ingestion of a carbohydrate load by, and treating microbial infections by using compds. I. Libraries of compds are prepared having variable R7 for which μ and κ receptor and α-glucosidase inhibition data (IC50s) are tabulated.

IT 196101-74-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of selectively N-alkylated peptidomimetic compds. and combinatorial libraries)

RN 196101-74-3 ZCAPLUS
CN 1H-Indole-3-propanamide, α-amino-N-[(3R)-4-hydroxy-3-pyrrolidinyl]-N,1-bis(2-naphthalenylmethyl)-, (αS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

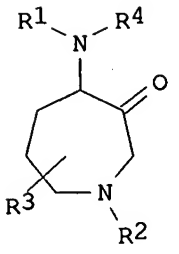
L4 ANSWER 63 OF 76 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:456887 ZCAPLUS
DOCUMENT NUMBER: 133:89444
TITLE: Preparation of 4-amino-azepan-3-one protease inhibitors
INVENTOR(S): Marquis, Robert Wells, Jr.; Ru, Yu; Veber, Daniel Frank; Cummings, Maxwell David; Thompson, Scott Kevin; Yamashita, Dennis
PATENT ASSIGNEE(S): Smithkline Beecham Corp., USA
SOURCE: PCT Int. Appl., 273 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000038687	A1	20000706	WO 1999-US30730	19991221
W: AE, AL, AU, BA, BB, BG, BR, CA, CN, CZ, EE, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2356671	A1	20000706	CA 1999-2356671	19991221
BR 9916488	A	20011009	BR 1999-16488	19991221
EP 1158986	A1	20011205	EP 1999-963112	19991221
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
TR 200101869	T2	20020121	TR 2001-200101869	19991221
HU 200104768	A2	20020429	HU 2001-4768	19991221
JP 2002533397	T	20021008	JP 2000-590640	19991221
AU 768565	B2	20031218	AU 2000-19411	19991221
NZ 511710	A	20031219	NZ 1999-511710	19991221
EP 1384713	A1	20040128	EP 2003-76211	19991221
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY				
ZA 2001004208	A	20020523	ZA 2001-4208	20010523
IN 2001MN00605	A	20050304	IN 2001-MN605	20010529
US 2003144175	A1	20030731	US 2001-881334	20010614
NO 2001003124	A	20010622	NO 2001-3124	20010622
NO 318910	B1	20050523		
MX 2001PA06613	A	20011203	MX 2001-PA6613	20010626
US 2002147188	A1	20021010	US 2002-74940	20020213
US 2003044399	A1	20030306	US 2002-74639	20020213
US 2003225061	A1	20031204	US 2003-404142	20030401
US 2004002487	A1	20040101	US 2003-404716	20030401
AU 2003261482	A1	20031204	AU 2003-261482	20031106
US 2005256104	A1	20051117	US 2005-152745	20050614
PRIORITY APPLN. INFO.:			US 1998-113636P	P 19981223
			US 1999-164581P	P 19991110
			AU 2000-19411	A3 19991221
			EP 1999-963112	A3 19991221
			WO 1999-US30730	W 19991221
			US 2000-593845	B2 20000614
			US 2000-653815	A1 20000901

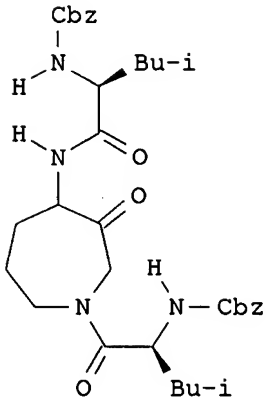
US 2001-881334 A1 20010614
US 2002-74940 A1 20020213
US 2003-404716 B1 20030401

OTHER SOURCE(S): MARPAT 133:89444

GI



I



II

AB The title compds. [I; R1 = COCR13NR11R12, COCR13XR15, COCH2R13; R2 = H, alkyl, cycloalkylalkyl, etc.; R3 = H, alkyl, cycloalkylalkyl, etc.; R4 = H, alkyl, arylalkyl, etc.; R11 = H, alkyl, arylalkyl, etc.; R12 = H, alkyl, cycloalkyl, etc.; R13 = H, alkyl, alkenyl, etc.; R15 = H, alkyl, alkenyl, etc.] which inhibit proteases (no data), including cathepsin K, and are useful for treating diseases of excessive bone loss or cartilage or matrix degradation including osteoporosis, gingival disease including gingivitis and periodontitis, arthritis, more specifically, osteoarthritis and rheumatoid arthritis, Paget's disease, hypercalcemia of malignancy, and metabolic bone disease, were prepared E.g., a multi-step synthesis of compound II was given. Compds. I are effective at 0.4-400 mg/kg/day.

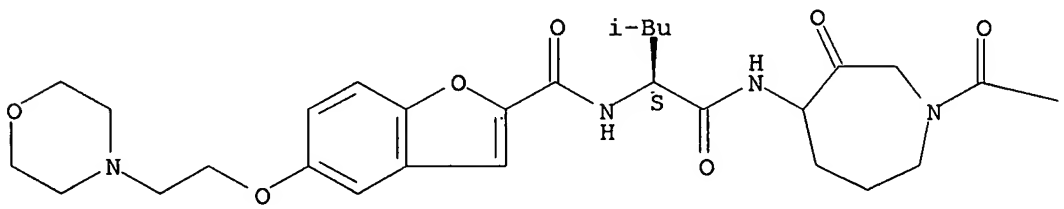
IT 281214-81-1P 281214-85-5P 281214-88-8P
281214-92-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of 4-amino-azepan-3-one protease inhibitors)

RN 281214-81-1 ZCAPLUS

CN 1H-Azepine-1-carboxylic acid, hexahydro-4-[[(2S)-4-methyl-2-[[[5-[2-(4-morpholinyl)ethoxy]-2-benzofuranyl]carbonyl]amino]-1-oxopentyl]amino]-3-oxo-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

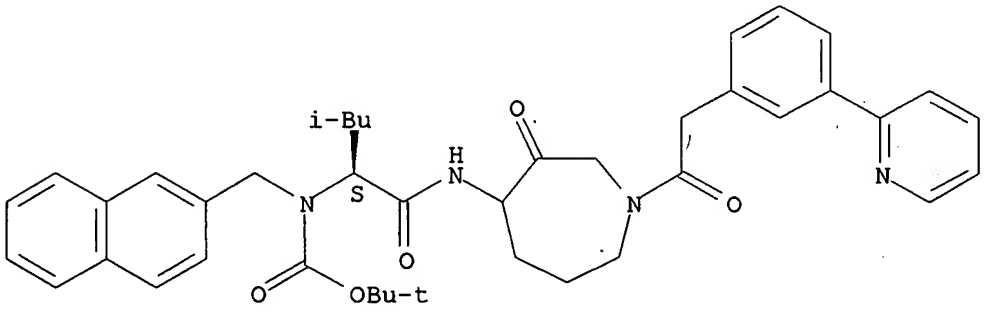


PAGE 1-B

—OBu-t

RN 281214-85-5 ZCAPLUS
CN Carbamic acid, [(1S)-1-[[[hexahydro-3-oxo-1-[[3-(2-pyridinyl)phenyl]acetyl]-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl](2-naphthalenylmethyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

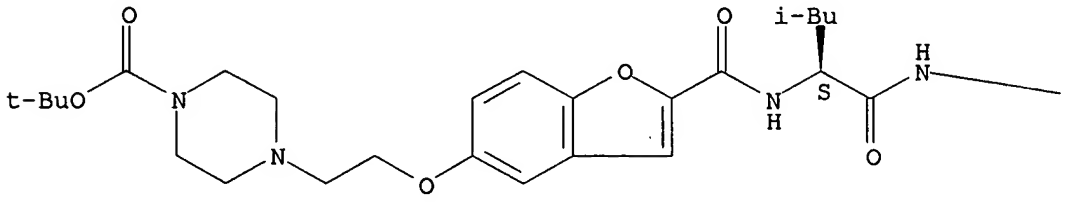
Absolute stereochemistry.



RN 281214-88-8 ZCAPLUS
CN 1-Piperazinecarboxylic acid, 4-[2-[[2-[[[(1S)-1-[[[hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]amino]carbonyl]-5-benzofuranyl]oxy]ethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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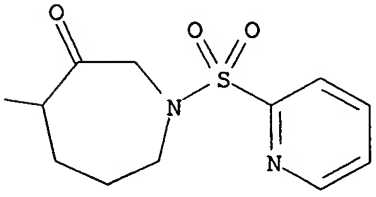
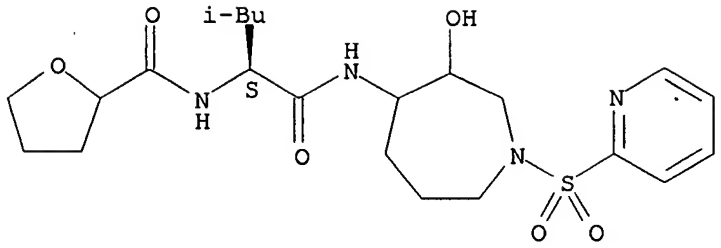


RN 281214-92-4 ZCAPLUS



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 64 OF 76 ZCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:596173 ZCAPLUS
DOCUMENT NUMBER: 132:3544
TITLE: Synthesis and Characterization of Bradykinin B2 Receptor Agonists Containing Constrained Dipeptide Mimics
AUTHOR(S): Amblard, Muriel; Daffix, Isabelle; Berge, Gilbert; Calmes, Monique; Dodey, Pierre; Pruneau, Didier; Paquet, Jean-Luc; Luccarini, Jean-Michel; Belichard, Pierre; Martinez, Jean
CORPORATE SOURCE: Laboratoire des Aminoacides Peptides et Proteines, Universites Montpellier I et II Faculte de Pharmacie, Montpellier, 34060, Fr.
SOURCE: Journal of Medicinal Chemistry (1999), 42(20), 4193-4201
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We have previously shown that substitution of the D-Tic-Oic dipeptide by a (3S)-[amino]-5-(carbonylmethyl)-2,3-dihydro-1,5-benzothiazepin-4(5H)-one (D-BT) moiety in the bradykinin B2 receptor antagonist HOE 140 resulted in a full potent and selective bradykinin B2 receptor agonist (H-DArg-Arg-Pro-Hyp-Gly-Thi-Ser-D-BT-Arg-OH, JMV 1116) exhibiting a high affinity for the human receptor (Ki 0.7 nM). In the present study, we have investigated the effects of replacement of the D-Tic-Oic moiety by various constrained dipeptide mimetics. The resulting compds. were tested for their binding affinity toward the cloned human B2 receptor and for their functional interaction with the bradykinin-induced contraction of isolated human umbilical vein. Subsequently, we have designed novel bradykinin B2 receptor agonists which are likely to be resistant to enzymic cleavage by endopeptidases and which might represent interesting new pharmacol. tools. In an attempt to increase the potency of compound JMV 1116, both its N-terminal part and the D-BT moiety were modified. Substitution of the D-arginine residue by a L-lysine residue led to a 10-fold more potent bradykinin B2 ligand [compound JMV 1465 (Kι 0.07 nM)], retaining full agonist activity on human umbilical vein. Substitution of the D-BT moiety by a (3S)-[amino]-5-(carbonylmethyl)-2,3-dihydro-8-methyl-1,5-benzothiazepin-4(5H)-one [D-BT(Me)] moiety led to compound JMV 1609 which exhibited a higher agonist activity (pD2 = 7.4) than JMV 1116 (pD2 = 6.8).

IT 250682-65-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation, binding affinity, functional interaction of bradykinin B2

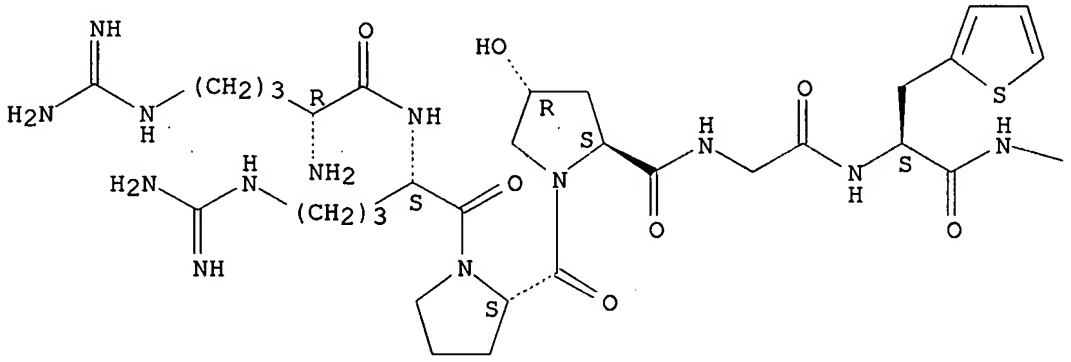
analogs and bradykinin B2 receptor agonists containing constrained dipeptide mimics)

RN 250682-65-6 ZCAPLUS

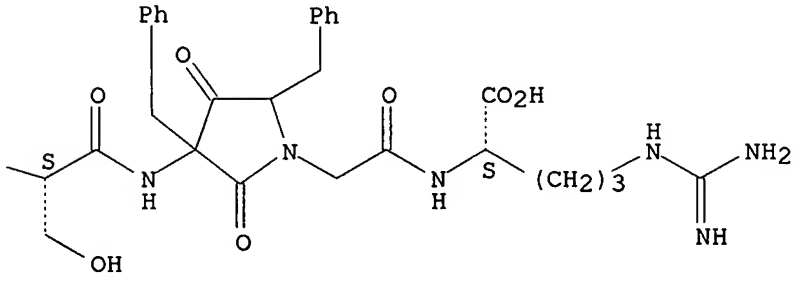
CN L-Arginine, D-arginyl-L-arginyl-L-prolyl-(4R)-4-hydroxy-L-prolylglycyl-3-(2-thienyl)-L-alanyl-L-seryl-3-amino-2,4-dioxo-3,5-bis(phenylmethyl)-1-pyrrolidineacetyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 65 OF 76 ZCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:578847 ZCAPLUS

DOCUMENT NUMBER: 132:152114

TITLE: Design and synthesis of potent and selective inhibitors of the osteoclast-specific cysteine protease, cathepsin K

AUTHOR(S): Veber, D. F.; Marquis, R. W.; Ru, Y.; Yamashita, D. S.; Oh, H.-J.; Thompson, S. K.; Halbert, S. M.; Carr, T. J.; Gleason, J. G.; Tomaszek, T. A.; Levy, M. A., Jr.; Bossard, M.; Tew, D. G.; James, I. E.; Briand, J.; Carr, S. A.; Zymbryki, D.; Lee-Rykaczewski, L.; Desjarlais, R. L.; McQueney, M. S.; D'Alessio, K. J.; Zhao, B.; Janson, C. A.; Abdel-Meguid, S. S.; Smith, W. W.

CORPORATE SOURCE: SmithKline Beecham Pharmaceuticals, King of Prussia, PA, 19406, USA

SOURCE: Peptide Science: Present and Future, Proceedings of

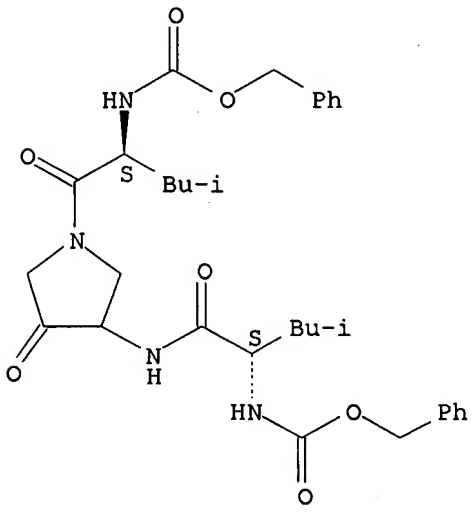
the International Peptide Symposium, 1st, Kyoto, Nov. 30-Dec. 5, 1997 (1999), Meeting Date 1997, 628-630. Editor(s): Shimonishi, Yasutsugu. Kluwer: Dordrecht, Neth.
CODEN: 68BYA5
DOCUMENT TYPE: Conference
LANGUAGE: English

AB A symposium on the authors' work in designing six peptidomimetic compds. for use as cathepsin K inhibitors.

IT 190141-90-3 190141-92-5
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(design and synthesis of potent and selective inhibitors of the osteoclast-specific cysteine protease cathepsin k)

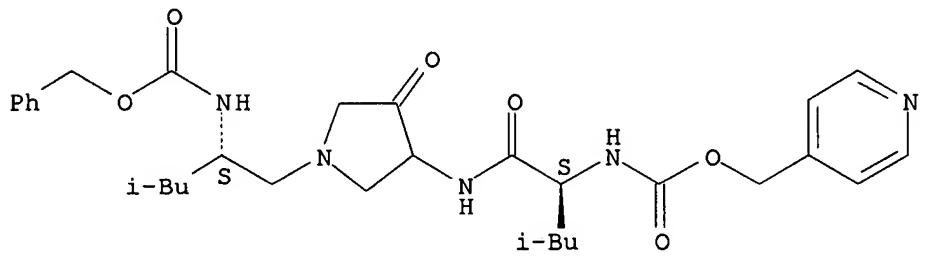
RN 190141-90-3 ZCAPLUS
CN Carbamic acid, [(1S)-3-methyl-1-[[3-[[(2S)-4-methyl-1-oxo-2-[[(phenylmethoxy)carbonyl]amino]pentyl]amino]-4-oxo-1-pyrrolidinyl]carbonyl]butyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 190141-92-5 ZCAPLUS
CN Carbamic acid, [(1S)-3-methyl-1-[[4-[[(2S)-4-methyl-1-oxo-2-[[(4-pyridinylmethoxy)carbonyl]amino]pentyl]amino]-3-oxo-1-pyrrolidinyl]methyl]butyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

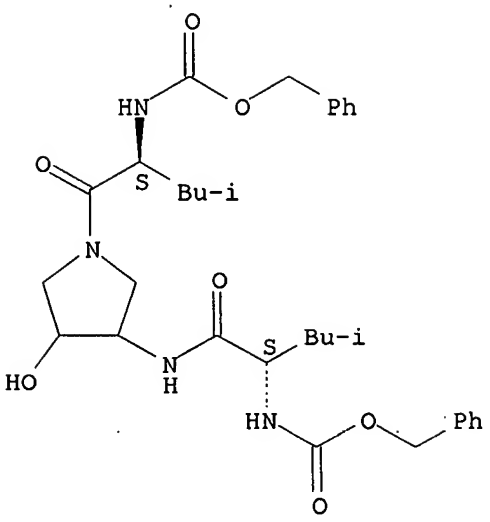
L4 ANSWER 66 OF 76 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:520368 ZCAPLUS
DOCUMENT NUMBER: 129:269956
TITLE: Conformationally constrained 1,3-diamino ketones: a series of potent inhibitors of the cysteine protease cathepsin K
AUTHOR(S): Marquis, Robert W.; Yamashita, Dennis S.; Ru, Yu; LoCastro, Stephen M.; Oh, Hye-Ja; Erhard, Karl F.; DesJarlais, Renee L.; Head, Martha S.; Smith, Ward W.; Zhao, Baoguang; Janson, Cheryl A.; Abdel-Meguid, Sherin S.; Tomaszek, Thaddeus A.; Levy, Mark A.; Veber, Daniel F.
CORPORATE SOURCE: Departments of Medicinal Chemistry Structural and Physical Chemistry Structural Biology and Molecular Recognition, SmithKline Beecham Pharmaceuticals, King of Prussia, PA, 19406, USA
SOURCE: Journal of Medicinal Chemistry (1998), 41(19), 3563-3567
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB To design more potent inhibitors of cathepsin K, the authors incorporated a 1,3-bis(Cbz-Leu-amino)-2-propanone inhibitor template into conformationally constrained ring systems. Introduction of a conformational constraint was used to capture bioactive orientations of mols. A variety of structure-activity relations are reported. Incorporation of the sulfonamide into the peptidomimetic gave the potent 4-phenoxybenzenesulfonamide derivative This modification has removed most of the structural liabilities commonly associated with peptide amide linkages.

IT 190142-02-0P 203501-30-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PNU (Preparation, unclassified); PRP (Properties); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(conformationally constrained 1,3-diamino ketones as potent inhibitors of the cysteine protease cathepsin K)

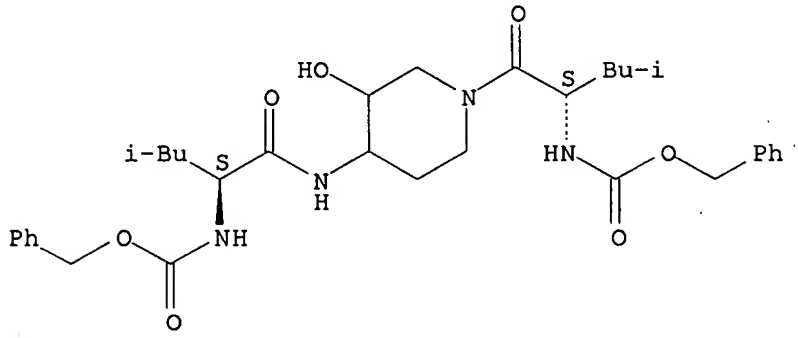
RN 190142-02-0 ZCAPLUS
CN Carbamic acid, [(1S)-1-[[3-hydroxy-4-[[(2S)-4-methyl-1-oxo-2-[[(phenylmethoxy)carbonyl]amino]pentyl]amino]-1-pyrrolidinyl]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



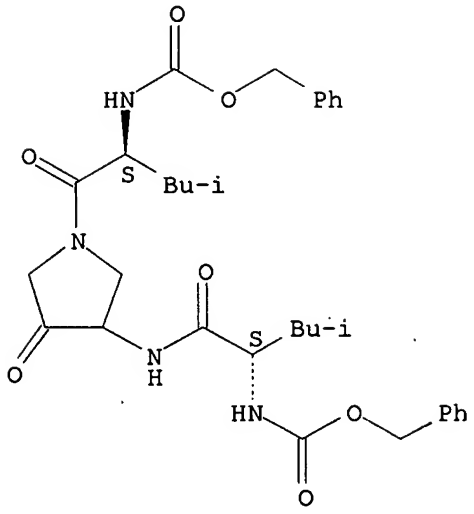
RN 203501-30-8 ZCAPLUS
CN Carbamic acid, [(1S)-1-[[3-hydroxy-4-[[(2S)-4-methyl-1-oxo-2-[[(phenylmethoxy)carbonyl]amino]pentyl]amino]-1-piperidinyl]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



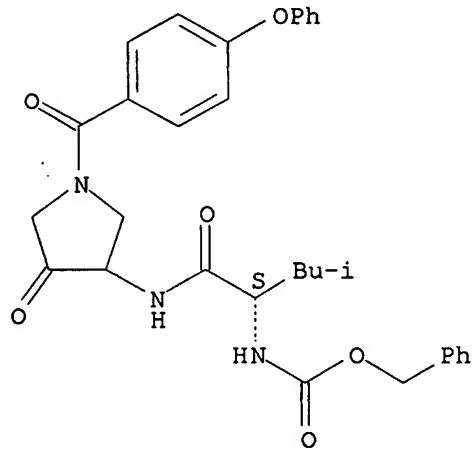
IT 190141-90-3P 203498-26-4P 203499-12-1P
203499-83-6P 203499-88-1P 213825-00-4P
213825-02-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PNU (Preparation, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(conformationally constrained 1,3-diamino ketones as potent inhibitors of the cysteine protease cathepsin K)
RN 190141-90-3 ZCAPLUS
CN Carbamic acid, [(1S)-3-methyl-1-[[3-[[(2S)-4-methyl-1-oxo-2-[[(phenylmethoxy)carbonyl]amino]pentyl]amino]-4-oxo-1-pyrrolidinyl]carbonyl]butyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



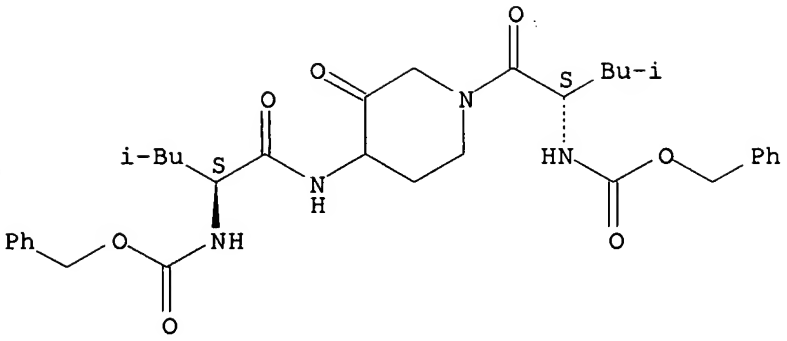
RN 203498-26-4 ZCAPLUS
CN Carbamic acid, [(1S)-3-methyl-1-[[[4-oxo-1-(4-phenoxybenzoyl)-3-pyrrolidinyl]amino]carbonyl]butyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



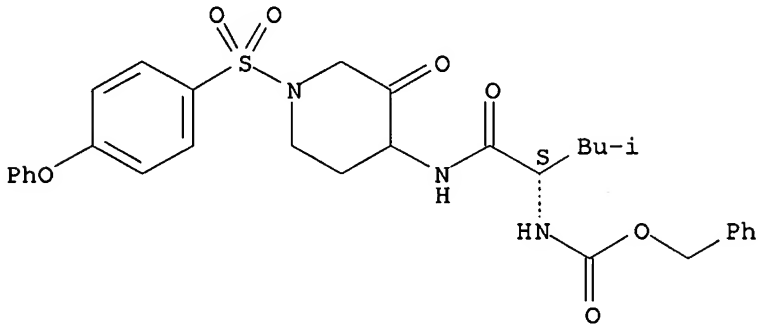
RN 203499-12-1 ZCAPLUS
CN Carbamic acid, [(1S)-3-methyl-1-[[4-[[(2S)-4-methyl-1-oxo-2-[[(phenylmethoxy)carbonyl]amino]pentyl]amino]-3-oxo-1-piperidinyl]carbonyl]butyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



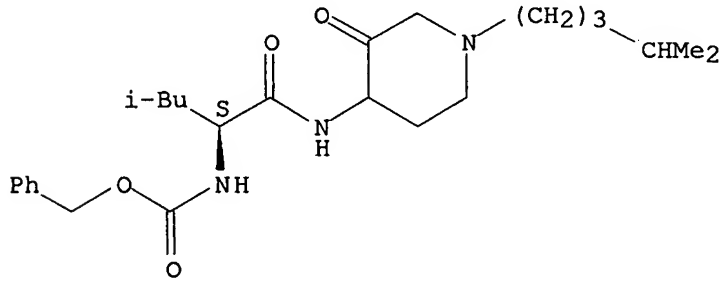
RN 203499-83-6 ZCAPLUS
CN Carbamic acid, [(1S)-3-methyl-1-[[[3-oxo-1-[(4-phenoxyphenyl)sulfonyl]-4-piperidinyl]amino]carbonyl]butyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



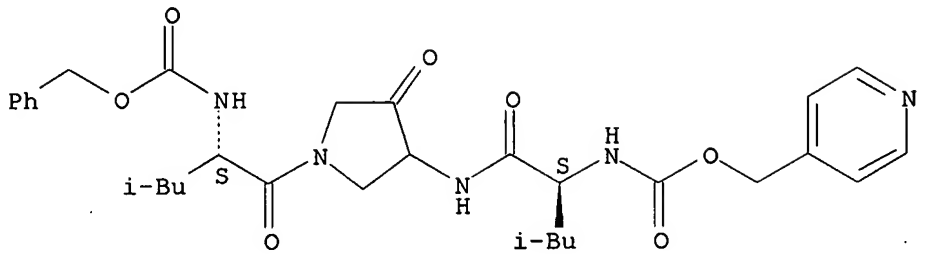
RN 203499-88-1 ZCAPLUS
CN Carbamic acid, [(1S)-3-methyl-1-[[[1-(4-methylpentyl)-3-oxo-4-piperidinyl]amino]carbonyl]butyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



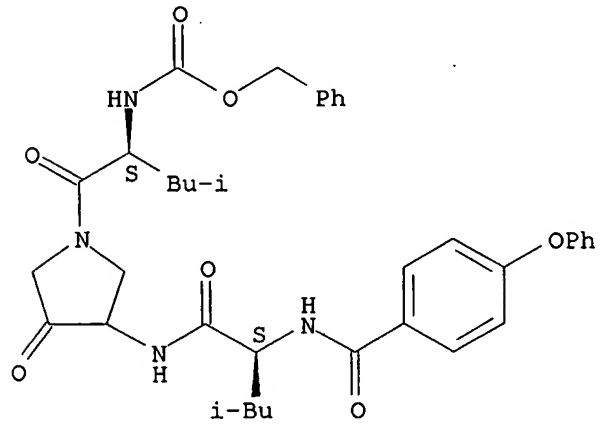
RN 213825-00-4 ZCAPLUS
CN Carbamic acid, [(1S)-3-methyl-1-[[[1-[(2S)-4-methyl-1-oxo-2-[[(phenylmethoxy)carbonyl]amino]pentyl]-4-oxo-3-pyrrolidinyl]amino]carbonyl]butyl]-, 4-pyridinylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 213825-02-6 ZCAPLUS
CN Carbamic acid, [(1S)-3-methyl-1-[[3-[[(2S)-4-methyl-1-oxo-2-[(4-phenoxybenzoyl)amino]pentyl]amino]-4-oxo-1-pyrrolidinyl]carbonyl]butyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 67 OF 76 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:197471 ZCAPLUS
DOCUMENT NUMBER: 128:265374
TITLE: Combinatorial approach for generating novel coordination complexes
INVENTOR(S): Jacobsen, Eric N.; Francis, Matthew B.; Finney, Nathaniel S.
PATENT ASSIGNEE(S): President and Fellows of Harvard College, USA; Jacobsen, Eric N.; Francis, Matthew B.; Finney, Nathaniel S.
SOURCE: PCT Int. Appl., 89 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9812156	A1	19980326	WO 1997-US16740	19970919

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,

DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT,
RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ,
VN, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR,
GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA,
GN, ML, MR, NE, SN, TD, TG

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US 6489093	B1	20021203	US 1997-933714		19970919
PRIORITY APPLN. INFO.:			US 1996-26432P-	P	19960920
			WO 1997-US16740	W	19970919

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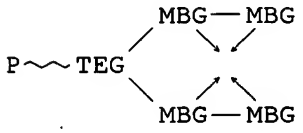

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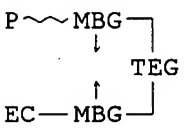


II

AB The present invention provides methods and compns., i.e. synthetic libraries of binding moieties, for identifying compds. which bind to a metal atom or to non-metal ions, e.g., cationic or anionic mols. Thus, combinatorial libraries, e.g. I and II (P = TentaGel S amino resin polymer support; TEG = turn element group, i.e. di- or trifunctional cyclic amino alc. or cyclic amino acid; MBG = metal binding group, i.e. amino acid residue; EC = end capping group, i.e. acyl residue) were prepared and examined for their ability to coordinate transition metal ions. Thus, a 12,000 member combinatorial library P-NHCO(CH2)5NH-A-B-C-D [III; P-NH2 = TentaGel S amino resin polymer; A (position 1) = L- or D-Asp(OCMe3), L- or D-Ser(CMe3), L- or D-Met, L- or D-Tyr(CMe3), L- or D-phenylglycine, His(CPh3), Gly; C (position 2) = L-Asp(OCMe3), L-Ser(CMe3), L-Tyr(CMe3), L-His(CPh3), L-Met, L-Trp, Gly, L-phenylglycine, 4-piperidinecarboxylic acid; B (turn element) = 1-amino-2-carbonyloxycyclopentane stereoisomers, 1-amino-2-carbonyloxycyclohexane stereoisomers, 1-amino-2-carbonyloxyindane stereoisomers, L-Pro, D-pipecolinic acid; D (end cap) = RCO, tosyl, pyroglutamic acid, R = Me, CMe3, 1-naphthyl, CH2CO2Me, 2-pyridyl, 3,4-methylenedioxyphenyl, PhNH] was prepared using standard solid-phase peptide coupling techniques. Library III was tested for Ni2+ binding affinity by treatment with 2.5 + 10-4 M Ni(OAc)2 in MeOH followed by solution of dimethylglyoxime in MeOH to form a reddish-pink precipitate
trapped in the polymer matrix of about 6 of the 24,000 beads. Tag photolysis and anal. allowed the identification of the individual nickel-binding library members.

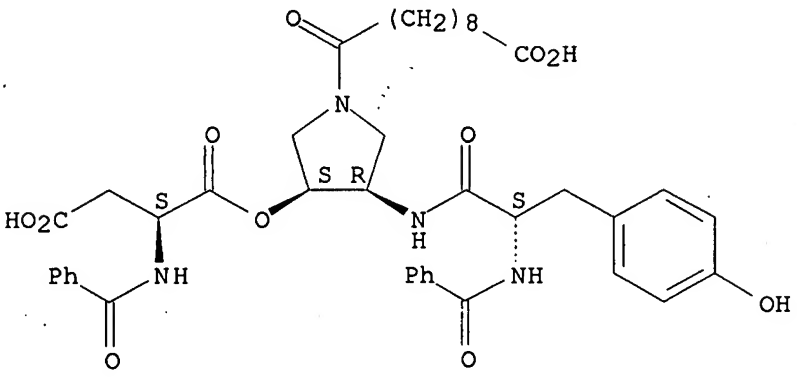
IT 205324-97-6DP, amide with TentaGel S resin 205324-98-7DP, amide with TentaGel S resin 205324-99-8DP, amide with TentaGel S resin 205325-00-4DP, amide with TentaGel S resin 205325-01-5DP, amide with TentaGel S resin 205325-02-6DP, amide with TentaGel S resin 205325-03-7DP, amide with TentaGel S resin 205325-04-8DP, amide with TentaGel S resin 205325-05-9DP, amide with TentaGel S resin
RL: CAT (Catalyst use); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(combinatorial approach for generating novel coordination complexes)

RN 205324-97-6 ZCAPLUS

CN L-Aspartic acid, N-benzoyl-, 1-[(3S,4R)-4-[[(2S)-2-(benzoylamino)-3-(4-

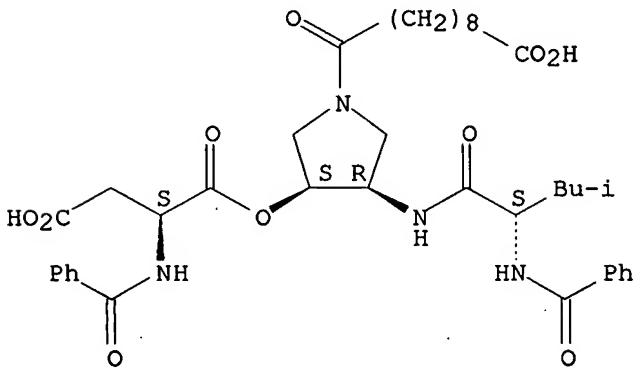
hydroxyphenyl)-1-oxopropyl]amino]-1-(9-carboxy-1-oxononyl)-3-pyrrolidinyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



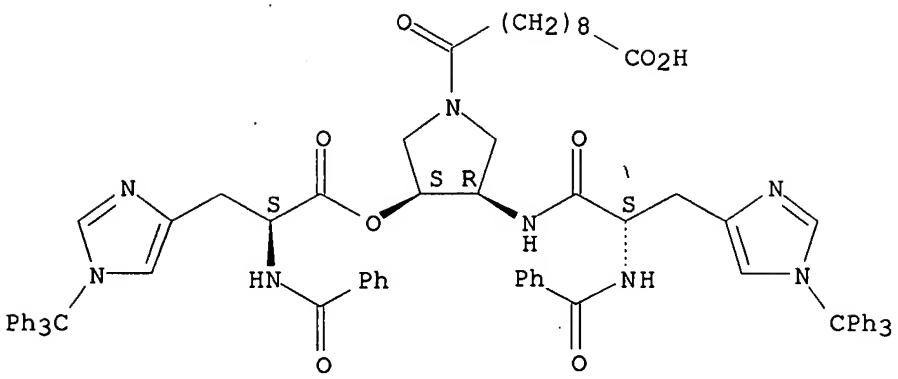
RN 205324-98-7 ZCAPLUS
CN L-Aspartic acid, N-benzoyl-, 1-[(3S,4R)-4-[[(2S)-2-(benzoylamino)-4-methyl-1-oxopentyl]amino]-1-(9-carboxy-1-oxononyl)-3-pyrrolidinyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



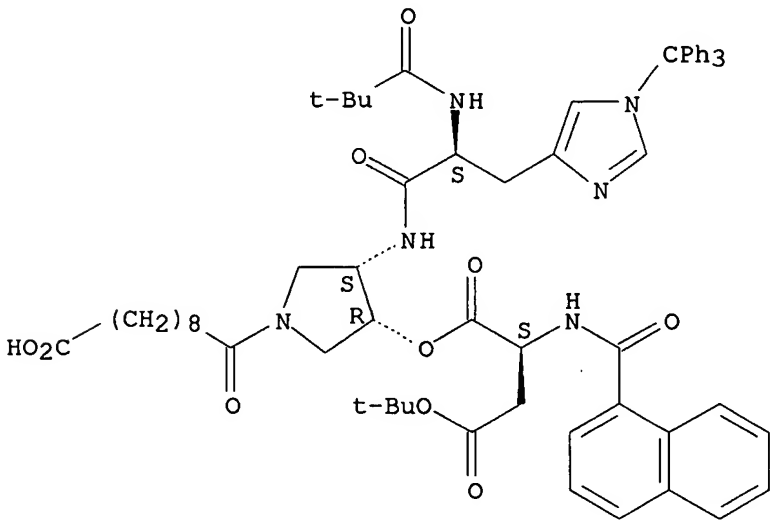
RN 205324-99-8 ZCAPLUS
CN L-Aspartic acid, N-benzoyl-, 1-[(3R,4R)-4-[[(2S,3S)-2-(benzoylamino)-3-methyl-1-oxopentyl]amino]-1-(9-carboxy-1-oxononyl)-3-pyrrolidinyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 205325-13-9 ZCAPLUS
CN L-Aspartic acid, N-(1-naphthalenylcarbonyl)-, 1-[(3R,4S)-1-(9-carboxy-1-oxononyl)-4-[[(2S)-2-[(2,2-dimethyl-1-oxopropyl)amino]-1-oxo-3-[1-(triphenylmethyl)-1H-imidazol-4-yl]propyl]amino]-3-pyrrolidinyl] 4-(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 68 OF 76 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:112238 ZCAPLUS
DOCUMENT NUMBER: 128:192935
TITLE: Preparation of heterocyclic peptide derivatives as cysteine protease inhibitors
INVENTOR(S): Marquis, Robert W., Jr.; Veber, Daniel F.; Ru, Yu; Lo, Castro Stephen
PATENT ASSIGNEE(S): Smithkline Beecham Corp., USA; Marquis, Robert W. Jr.; Veber, Daniel F.; Ru, Yu; Lo Castro, Stephen
SOURCE: PCT Int. Appl., 176 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9805336	A1	19980212	WO 1997-US13875		19970807
W: AL, AM, AU, BB, BG, BR, CA, CN, CZ, EE, GE, GH, HU, IL, IS, JP, KG, KP, KR, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, US, UZ, VN, YU, AZ, BY, KZ, RU, TJ, TM					
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
IN 1997DE02169	A	20050311	IN 1997-DE2169		19970804
AP 865	A	20000817	AP 1997-1054		19970806
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CA 2262668	A1	19980212	CA 1997-2262668		19970807
CA 2262668	C	20060509			
AU 9739726	A	19980225	AU 1997-39726		19970807
AU 721853	B2	20000713			
ZA 9707032	A	19980804	ZA 1997-7032		19970807
EP 936912	A1	19990825	EP 1997-937146		19970807
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HU 9902409	A2	19991129	HU 1999-2409		19970807
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BR 9711044	A	20001024	BR 1997-11044		19970807
JP 2000516920	T	20001219	JP 1998-508213		19970807
IL 128378	A	20031031	IL 1997-128378		19970807
AT 259352	T	20040215	AT 1997-937146		19970807
PT 936912	T	20040630	PT 1997-937146		19970807
ES 2213831	T3	20040901	ES 1997-937146		19970807
RO 120407	B1	20060130	RO 1999-137		19970807
SK 285127	B6	20060601	SK 1999-162		19970807
PL 191779	B1	20060731	PL 1997-331533		19970807
CZ 297294	B6	20061115	CZ 1999-362		19970807
TW 542825	B	20030721	TW 1997-86111564		19970922
BG 64412	B1	20050131	BG 1999-103144		19990203
NO 9900548	A	19990407	NO 1999-548		19990205
NO 317182	B1	20040906			
KR 2000029863	A	20000525	KR 1999-701027		19990206
HK 1022096	A1	20041105	HK 2000-101085		20000223
US 2002128476	A1	20020912	US 2001-836586		20010417
US 2004180927	A1	20040916	US 2004-789063		20040227
PRIORITY APPLN. INFO.:			US 1996-23742P	P	19960808
			US 1997-46867P	P	19970508
			WO 1997-US13875	W	19970807
			US 1999-230791	B1	19990208
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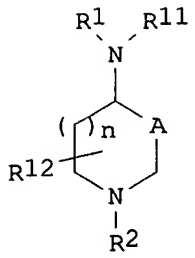
OTHER SOURCE(S): MARPAT 128:192935

GI



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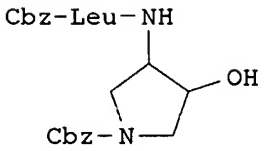
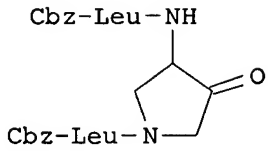


II



III

AB Title heterocycles I [A = CO, CH(OH); R11, R12, R9, R6 = = H, C1-6 alkyl, C3-6 cycloalkyl-C0-6 alkyl, Ar-C0-6 alkyl, Het-C0-6 alkyl; R1 = R4R10NCHR3Z, ARCHR9CO, 4-(Ph-Y)C6H4CO, dibenzofuran-2-sulfonyl; R2 = any group R11, R5CO, R5CS, R5SO2, R5O2C, R5R10NCO, R5R10NCS, adamantyl-CO, R6R7NCHR3-Z; R3 = H, C2-6 alkenyl, C2-6 alkynyl, Het, Ar, C1-6 alkyl (un)substituted by OR10, SR10, NR102, R10NCO2R5, CO2R10, CO2NR102, NC:NHNH2, Het, Ar; R4, R7 = any group R11, R5CO, R5CS, R5SO2, R5O2C, R5R10NCO, R5R10NCS, R10HNCHR10CO, R5O2CNR10CHR10CO; R5 = C3-6 cycloalkyl-C0-6 alkyl, Ar-C0-6 alkyl, Het-C0-6 alkyl, Ar-C0-6 alkoxy, Het-C0-6 alkoxy, C1-6 alkyl (un)substituted by OR10, SR10, NR102, R10NCO2R5, CO2R10, CO2NR102, NC:NHNH2, Het, Ar; NR6R7 = pyrrolidino, piperidino, morpholino; R10 = H, C1-6 alkyl, Ar-C0-6 alkyl, Het-C0-6 alkyl; Y = bond, O; Z = CO, CH2; n = 0-2; Ar = aryl, Het = heterocyclyl] or a pharmaceutically acceptable salt thereof, are inhibitors of cysteine proteases, particularly cathepsin K, and are useful in the treatment of diseases in which inhibition of bone loss is a factor. Thus, coupling of 1-tert-butoxycarbonyl-trans-3-amino-4-hydroxypyrrolidine (preparation given) with Cbz-Leu-OH (Cbz = PhCH2O2C), followed by deprotection with HCl in EtOAc and further coupling with Cbz-Leu-OH gave trans-pyrrolidinol II. Jones oxidation of II gave desired title compound III.

IT 190142-02-0P 190142-03-1P 190142-05-3P
190142-07-5P 203500-70-3P 203501-16-0P
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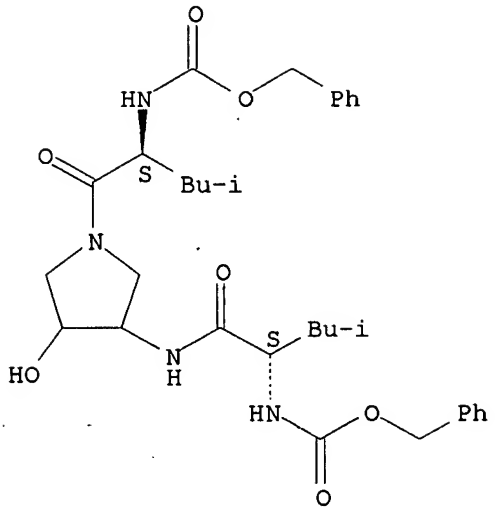
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of heterocyclic peptide derivs. as cysteine protease inhibitors)

RN 190142-02-0 ZCAPLUS

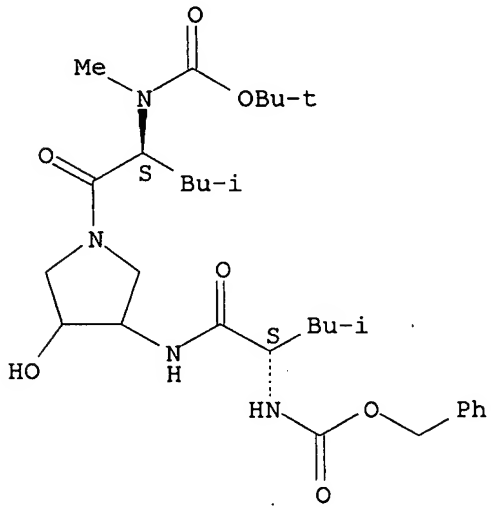
CN Carbamic acid, [(1S)-1-[[3-hydroxy-4-[[(2S)-4-methyl-1-oxo-2-[[(phenylmethoxy)carbonyl]amino]pentyl]amino]-1-pyrrolidinyl]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



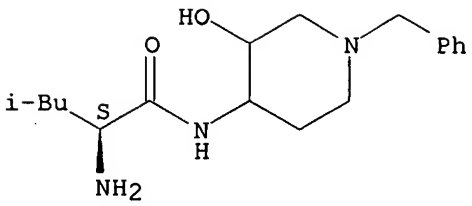
RN 190142-03-1 ZCAPLUS
CN Carbamic acid, [1-[[3-hydroxy-4-[[4-methyl-1-oxo-2-[[(phenylmethoxy)carbonyl]amino]pentyl]amino]-1-pyrrolidinyl]carbonyl]-3-methylbutyl]methyl-, 1,1-dimethylethyl ester, [1(S),4(S)]-[partial]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 190142-05-3 ZCAPLUS
CN 1-Pyrrolidinecarboxylic acid, 3-hydroxy-4-[[4-methyl-1-oxo-2-[[(4-pyridinylmethoxy)carbonyl]amino]pentyl]amino]-, 1,1-dimethylethyl ester, [4(S)]-[partial]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 69 OF 76 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:618263 ZCAPLUS
DOCUMENT NUMBER: 127:263064
TITLE: Preparation of selectively N-alkylated peptidomimetic combinatorial libraries and compounds as analgesics and antidiabetics
INVENTOR(S): Dorner, Barbara; Ostresh, John M.; Dooley, Collette T.; Eichler, Jutta; Houghten, Richard A.
PATENT ASSIGNEE(S): Torrey Pines Institute for Molecular Studies, USA
SOURCE: PCT Int. Appl., 153 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9733174	A1	19970912	WO 1997-IB349	19970305
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
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AU 9720405	A	19970922	AU 1997-20405	19970305
AU 720632	B2	20000608		
EP 890101	A1	19990113	EP 1997-908448	19970305
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JP 2001502293	T	20010220	JP 1997-531626	19970305
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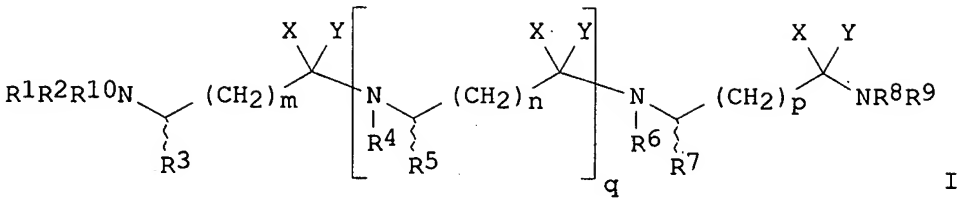

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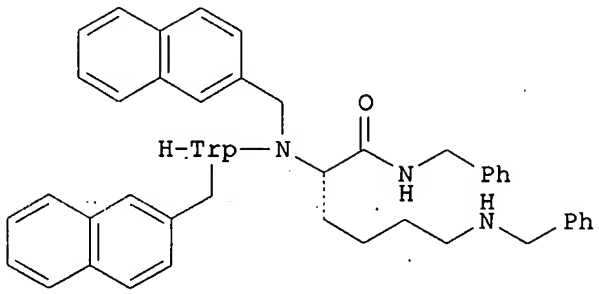


II

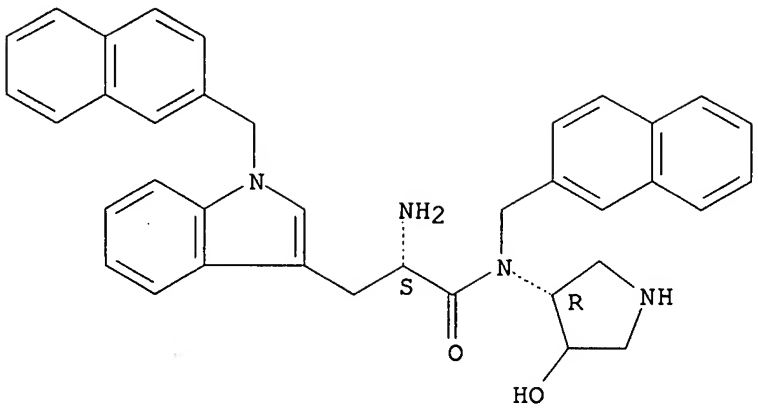
AB The instant invention is directed to a single, selectively N-alkylated compound I [R1, R2 = independently H, amino protecting group, C1-12 acyl, C3-10 cycloalkyl, C3-6 heterocyclyl, C1-12 (un)substituted alkyl, C7-16 (un)substituted alkylaryl, C6-15 (un)substituted alkylheterocyclyl; R3, R5, R7 = independently H, C1-12 (un)substituted alkyl, (un)substituted Ph, C7-16 (un)substituted alkylaryl, (un)substituted C6-15 alkylheterocyclyl; R4, E6, R8 = independently C1-18 substituent group; R9 = H, solid support; R10 = optionally present as C1-18 substituent group when R1 and R2 ≠ H, protecting group, C1-12 acyl; m, n, p = independently 0-5; q = 0-3; the stereochem. of carbons bound to R3, R5, and R7 are independently R, S, or a mixture of the two; with the proviso that either R1 or R2 can be taken with R3, R4 can be taken with R5, or R6 can be taken with R7, resp. and independently to form a substituted or unsubstituted pyrrolidine ring; X = Y = H;, XY = O] and pharmaceutically acceptable salts, solvate, or hydrate thereof, and libraries of such compds. Furthermore, the instant invention is directed to methods of effecting analgesia, a decrease in the postprandial rise in the blood glucose levels of a mammal after ingestion of a carbohydrate load by said mammal, and treating microbial infections, utilizing such a single compound I in conjunction with a pharmaceutically-acceptable carrier. Also, the instant invention is directed to methods for selective alkylation, positional scanning and iterative synthetic and screening technologies. Thus, dipeptide amide II was prepared via a solid-phase method that included an on-resin alkylation step. II inhibited α-glucosidase in an in vitro assay with IC50 = 19 μM.

IT 196101-74-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of selectively N-alkylated peptidomimetic combinatorial libraries and compds. as analgesics and antidiabetics)

RN 196101-74-3 ZCAPLUS

CN 1H-Indole-3-propanamide, α-amino-N-[(3R)-4-hydroxy-3-pyrrolidinyl]-N,1-bis(2-naphthalenylmethyl)-, (αS)- (9CI) (CA INDEX NAME)

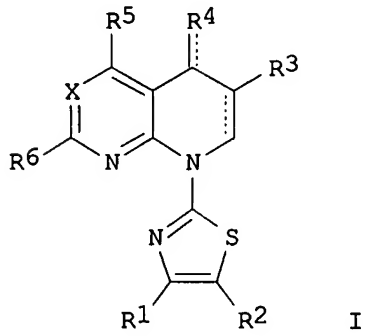
Absolute stereochemistry.



L4 ANSWER 70 OF 76 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:594555 ZCAPLUS
DOCUMENT NUMBER: 127:288165
TITLE: Antitumor compounds
INVENTOR(S): Tomita, Kyoji; Chiba, Katsumi; Kashimoto, Shigeki; Nakada, Katsuhisa; Shibamori, Koichiro; Chikugi, Yasutomo; Tajima, Masanori; Oue, Tomio
PATENT ASSIGNEE(S): Dainippon Pharmaceutical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 74 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
JP 09221424	A	19970826	JP 1996-351948		19961210
PRIORITY APPLN. INFO.:			JP 1995-347310	A	19951213
OTHER SOURCE(S):	MARPAT 127:288165				

GI



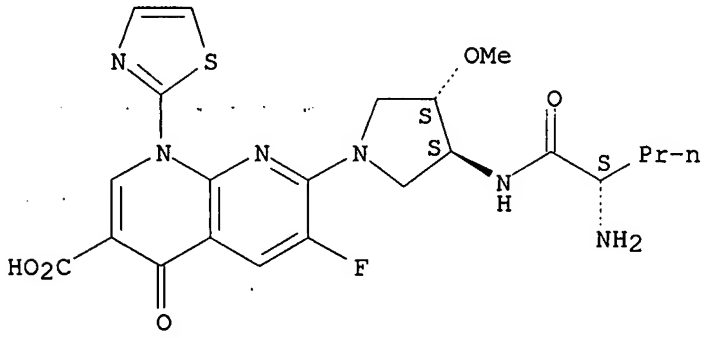
I

AB The title compds. (I; X = N or C-Rx, with Rx =H, halogen; R1, R2 = H, halogen; R3 = H, carboxyl; R4 = oxo, OH; R5 = H, amino; R6 = substituted cyclic amino groups) and their physiol. acceptable salts are claimed as antitumor drugs. Thus, I were prepared, and their antitumor activities were tested in animal models.

IT 177751-56-3P 177751-57-4P 177751-65-4P
196822-03-4P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(antitumor compds.)

RN 177751-56-3 ZCAPLUS
CN 1,8-Naphthyridine-3-carboxylic acid, 7-[3-[(2-amino-1-oxopentyl)amino]-4-methoxy-1-pyrrolidinyl]-6-fluoro-1,4-dihydro-4-oxo-1-(2-thiazolyl)-, monohydrochloride, [3S-[3α(R*),4β]]- (9CI) (CA INDEX NAME)

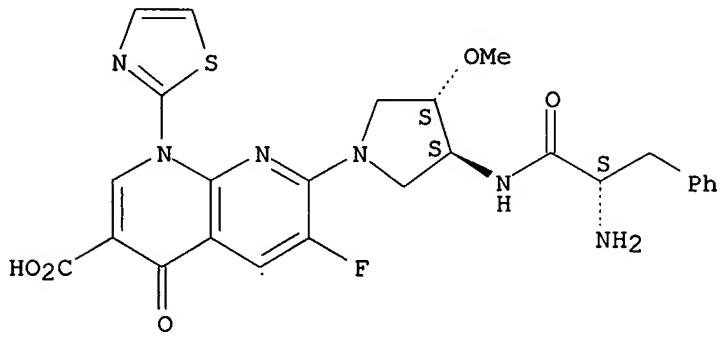
Absolute stereochemistry.



● HCl

RN 177751-57-4 ZCAPLUS
CN 1,8-Naphthyridine-3-carboxylic acid, 7-[3-[(2-amino-1-oxo-3-phenylpropyl)amino]-4-methoxy-1-pyrrolidinyl]-6-fluoro-1,4-dihydro-4-oxo-1-(2-thiazolyl)-, monohydrochloride, [3S-[3α(R*),4β]]- (9CI) (CA INDEX NAME)

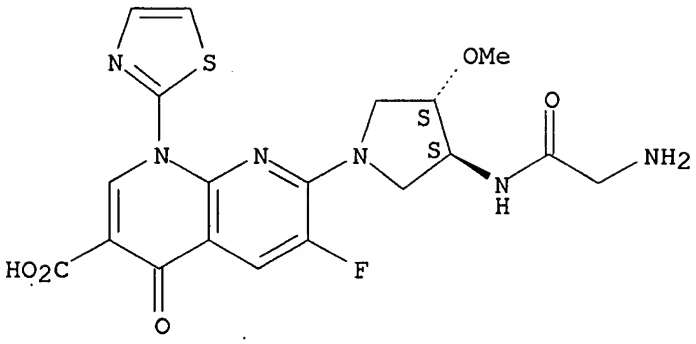
Absolute stereochemistry.



● HCl

RN 177751-65-4 ZCAPLUS
CN 1,8-Naphthyridine-3-carboxylic acid, 7-[3-[(aminoacetyl)amino]-4-methoxy-1-pyrrolidinyl]-6-fluoro-1,4-dihydro-4-oxo-1-(2-thiazolyl)-, monohydrochloride, (3S-trans)- (9CI) (CA INDEX NAME)

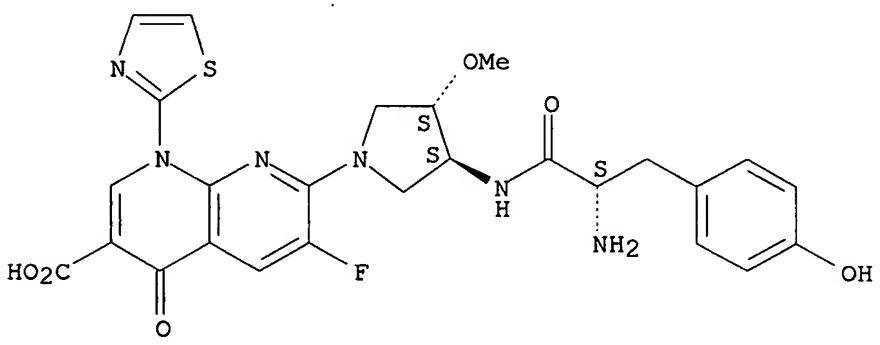
Absolute stereochemistry.



● HCl

RN 196822-03-4 ZCAPLUS
CN 1,8-Naphthyridine-3-carboxylic acid, 7-[3-[[2-amino-3-(4-hydroxyphenyl)-1-oxopropyl]amino]-4-methoxy-1-pyrrolidinyl]-6-fluoro-1,4-dihydro-4-oxo-1-(2-thiazolyl)-, monohydrochloride, [3S-[3α(R*),4β]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

L4 ANSWER 71 OF 76 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:390686 ZCAPLUS
DOCUMENT NUMBER: 127:5359
TITLE: Preparation and crystal structures of cathepsin K-inhibitor complexes
INVENTOR(S): Abdel-Mequid, Sherin Salaheldin; Carr, Thomas Joseph; Desjarlais, Renee Louise; Gallagher, Thimothy Francis; et al.
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 777 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9716177	A1	19970509	WO 1996-US17512	19961030
W: AL, AM, AU, BB, BG, BR, CA, CN, CZ, EE, GE, HU, IL, IS, JP, KG, KP, KR, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, US, UZ, VN, AZ, BY, KZ, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
ZA 9609078	A	19980429	ZA 1996-9078	19961029
IN 1996DE02359	A	20050311	IN 1996-DE2359	19961029
CA 2209109	A1	19970509	CA 1996-2209109	19961030
EP 804180	A1	19971105	EP 1996-943476	19961030
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI				
CN 1177293	A	19980325	CN 1996-192191	19961030
JP 10512300	T	19981124	JP 1997-517568	19961030
HU 9802488	A2	19990201	HU 1998-2488	19961030
CN 1207095	A	19990203	CN 1996-199284	19961030
BR 9607577	A	19990914	BR 1996-7577	19961030
NZ 324921	A	20000728	NZ 1996-324921	19961030
IN 1996DE02367	A	20050311	IN 1996-DE2367	19961030
AU 9712707	A	19970717	AU 1997-12707	19970212
AU 711014	B2	19991007		
WO 9749668	A1	19971231	WO 1997-US11501	19970613
W: JP, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 6274336	B1	20010814	US 1997-860255	19970626
NO 9703009	A	19970827	NO 1997-3009	19970627
IN 1997DE02169	A	20050311	IN 1997-DE2169	19970804
ZA 9707032	A	19980804	ZA 1997-7032	19970807
US 5998470	A	19991207	US 1999-290958	19990413
US 6232342	B1	20010515	US 1999-330451	19990611
PRIORITY APPLN. INFO.:			US 1995-8108P P	19951030
			US 1995-7473P P	19951122
			US 1995-8992P P	19951221
			US 1996-13747P P	19960320
			US 1996-13748P P	19960320
			US 1996-13764P P	19960320
			US 1996-17455P P	19960517
			US 1996-17892P P	19960517
			US 1996-20478P P	19960613
			US 1996-22047P P	19960722
			US 1996-23494P P	19960807
			US 1996-23742P P	19960808
			WO 1996-US17512 W	19961030
			US 1998-793915 A3	19980430

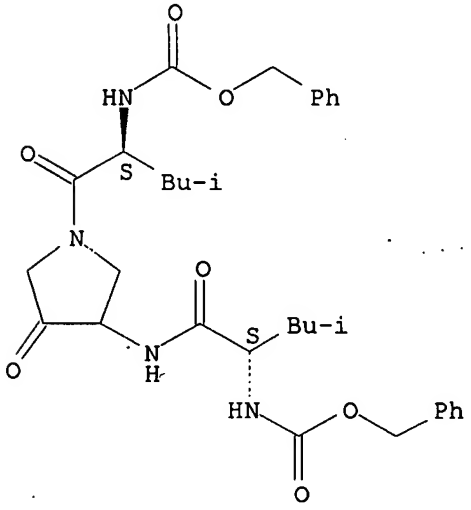
OTHER SOURCE(S): MARPAT 127:5359

AB A novel cathepsin K crystalline structure is identified. Also disclosed are methods of identifying inhibitors of this protease and methods of inhibiting cathepsin K using inhibitors with certain structural, phys. and spatial characteristics.

IT 190141-90-3P 190141-91-4P 190141-92-5P
190142-19-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of cathepsin K inhibitors and crystal structures of cathepsin K-inhibitor complexes)

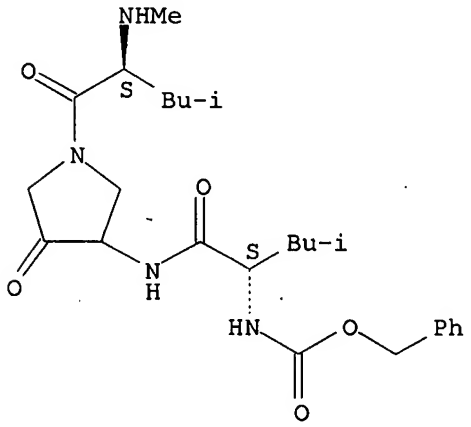
RN 190141-90-3 ZCAPLUS
CN Carbamic acid, [(1S)-3-methyl-1-[[3-[[(2S)-4-methyl-1-oxo-2-[[(phenylmethoxy)carbonyl]amino]pentyl]amino]-4-oxo-1-pyrrolidinyl]carbonyl]butyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 190141-91-4 ZCAPLUS
CN Carbamic acid, [3-methyl-1-[[[1-[4-methyl-2-(methylamino)-1-oxopentyl]-4-oxo-3-pyrrolidinyl]amino]carbonyl]butyl]-, phenylmethyl ester, monohydrochloride, [1(S),3(S)]-[partial]- (9CI) (CA INDEX NAME)

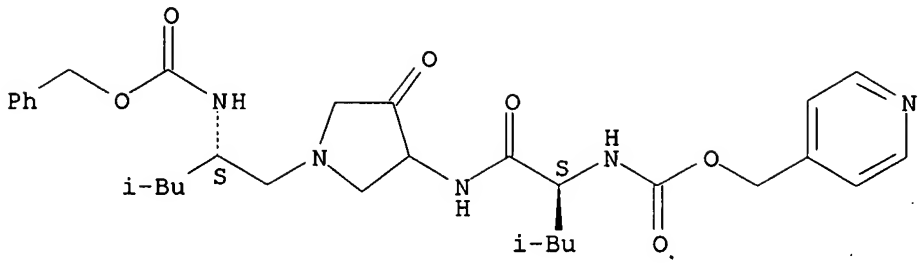
Absolute stereochemistry.



● HCl

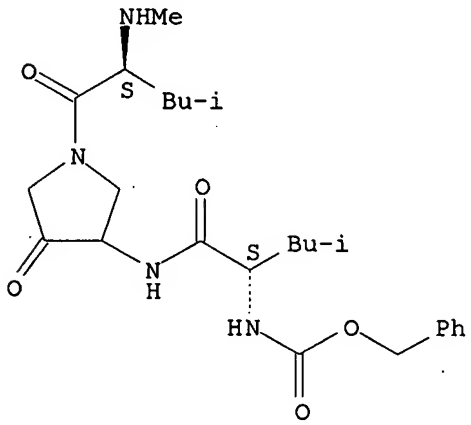
RN 190141-92-5 ZCAPLUS
CN Carbamic acid, [(1S)-3-methyl-1-[[4-[[(2S)-4-methyl-1-oxo-2-[[(4-pyridinylmethoxy)carbonyl]amino]pentyl]amino]-3-oxo-1-pyrrolidinyl]methyl]butyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



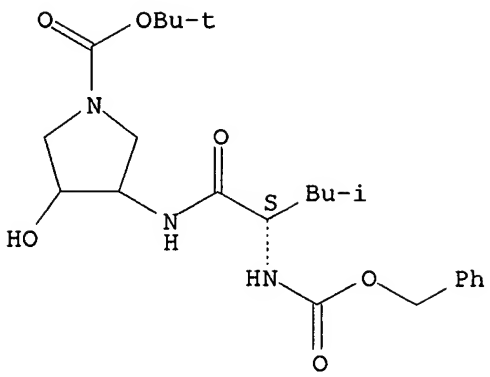
RN 190142-19-9 ZCAPLUS
CN Carbamic acid, [3-methyl-1-[[[1-[4-methyl-2-(methylamino)-1-oxopentyl]-4-oxo-3-pyrrolidinyl]amino]carbonyl]butyl]-, phenylmethyl ester, [1(S),3(S)]-[partial]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



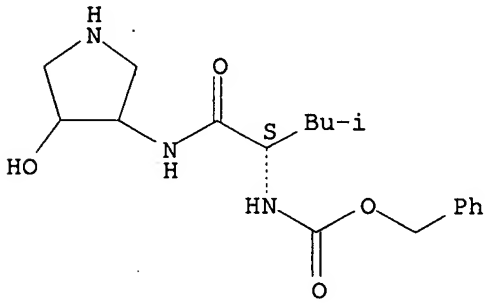
IT 190142-00-8P 190142-01-9P 190142-02-0P
190142-03-1P 190142-04-2P 190142-05-3P
190142-06-4P 190142-07-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of cathepsin K inhibitors and crystal structures of cathepsin K-inhibitor complexes)
RN 190142-00-8 ZCAPLUS
CN 1-Pyrrolidinecarboxylic acid, 3-hydroxy-4-[[(2S)-4-methyl-1-oxo-2-[[(phenylmethoxy)carbonyl]amino]pentyl]amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 190142-01-9 ZCAPLUS
CN Carbamic acid, [(1S)-1-[[(4-hydroxy-3-pyrrolidinyl)amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester, monohydrochloride (9CI) (CA INDEX NAME)

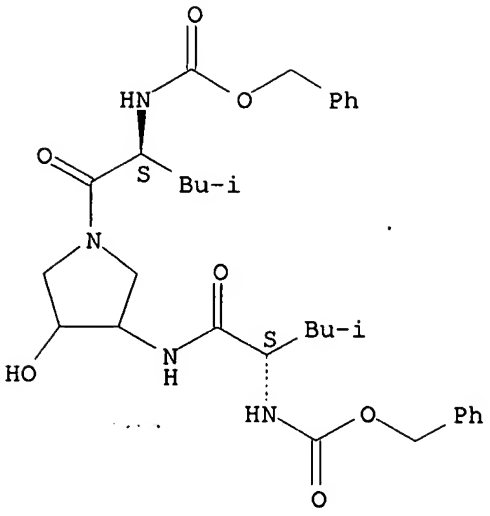
Absolute stereochemistry.



● HCl

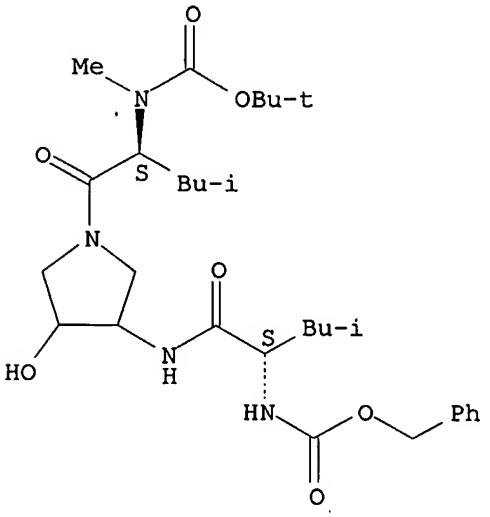
RN 190142-02-0 ZCAPLUS
CN Carbamic acid, [(1S)-1-[[3-hydroxy-4-[[(2S)-4-methyl-1-oxo-2-[[(phenylmethoxy)carbonyl]amino]pentyl]amino]-1-pyrrolidinyl]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



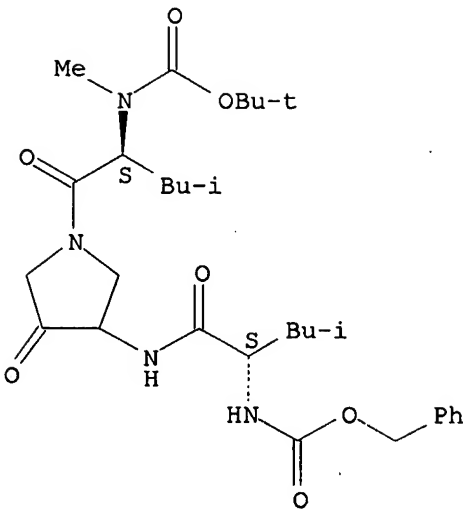
RN 190142-03-1 ZCAPLUS
CN Carbamic acid, [1-[[3-hydroxy-4-[[4-methyl-1-oxo-2-[[(phenylmethoxy)carbonyl]amino]pentyl]amino]-1-pyrrolidinyl]carbonyl]-3-methylbutyl]methyl-, 1,1-dimethylethyl ester, [1(S),4(S)]-[partial]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



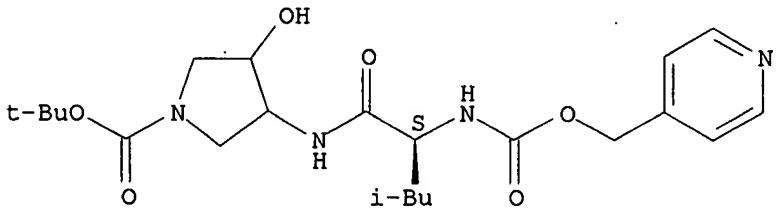
RN 190142-04-2 ZCAPLUS
CN Carbamic acid, methyl[3-methyl-1-[[3-[[4-methyl-1-oxo-2-[[(phenylmethoxy)carbonyl]amino]pentyl]amino]-4-oxo-1-pyrrolidinyl]carbonyl]butyl]-, 1,1-dimethylethyl ester, [1(S),3(S)]-[partial]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



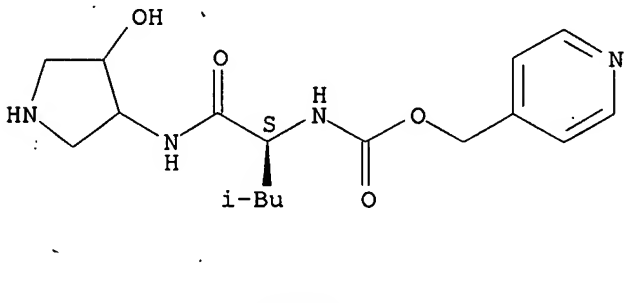
RN 190142-05-3 ZCAPLUS
CN 1-Pyrrolidinecarboxylic acid, 3-hydroxy-4-[[4-methyl-1-oxo-2-[[(4-pyridinylmethoxy)carbonyl]amino]pentyl]amino]-, 1,1-dimethylethyl ester, [4(S)]-[partial]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 190142-06-4 ZCAPLUS
CN Carbamic acid, [1-[[(4-hydroxy-3-pyrrolidinyl)amino]carbonyl]-3-methylbutyl]-, 4-pyridinylmethyl ester, monohydrochloride, [3(S)]-[partial]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

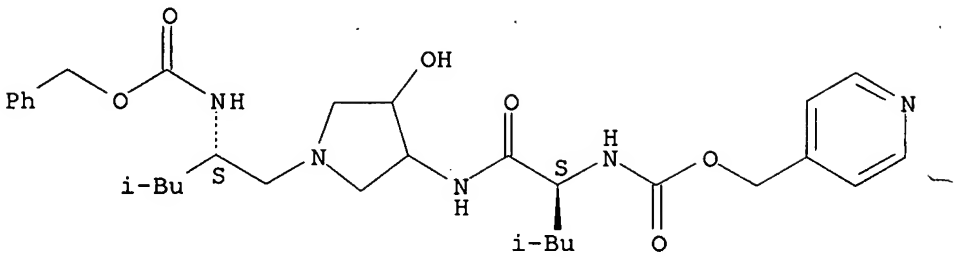


● HCl

RN 190142-07-5 ZCAPLUS
CN Carbamic acid, [1-[[3-hydroxy-4-[[4-methyl-1-oxo-2-[[(4-pyridinylmethoxy)carbonyl]amino]pentyl]amino]-1-pyrrolidinyl]methyl]-3-methylbutyl]-, phenylmethyl ester, [1(S),4(S)]-[partial]- (9CI) (CA INDEX

NAME)

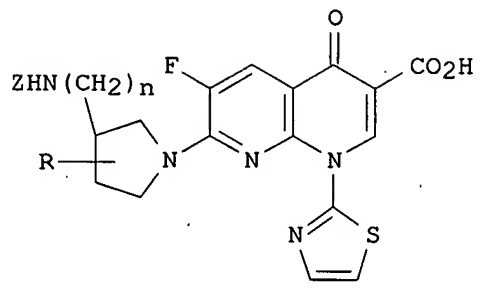
Absolute stereochemistry.



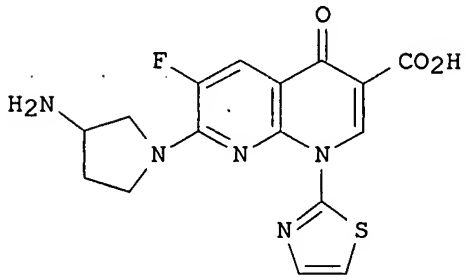
L4 ANSWER 72 OF 76 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:367330 ZCAPLUS
DOCUMENT NUMBER: 125:58488
TITLE: Preparation of naphthyridines as antitumor agents
INVENTOR(S): Nakada, Katsuhisa; Kashimoto, Shigeki; Tajima, Masanori; Ooe, Tomio; Chiba, Katsumi; Shibamori, Koichiro
PATENT ASSIGNEE(S): Dainippon Pharmaceutical Co, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 19 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 08073460	A	19960319	JP 1994-234228	19940902

PRIORITY APPLN. INFO.: JP 1994-234228 19940902
OTHER SOURCE(S): MARPAT 125:58488
GI



I



II

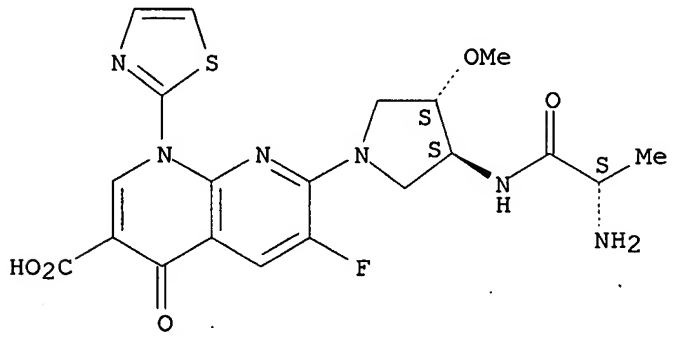
AB The title compds. I [R = H, alkyl, etc.; Z = H, alkyl, etc.; n = 0 or 1] and esters thereof are prepared The title compound II.HCl (preparation given) in vitro showed IC50 of 0.021 μg/mL against P388 mouse leukemic cells.

IT 177751-32-5P 177751-46-1P 177751-47-2P
177751-48-3P 177751-56-3P 177751-57-4P
177751-65-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of naphthyridines as antitumor agents)

RN 177751-32-5 ZCAPLUS

CN 1,8-Naphthyridine-3-carboxylic acid, 7-[3-[(2-amino-1-oxopropyl)amino]-4-methoxy-1-pyrrolidinyl]-6-fluoro-1,4-dihydro-4-oxo-1-(2-thiazolyl)-, monohydrochloride, [3S-[3α(R*),4β]]- (9CI) (CA INDEX NAME)

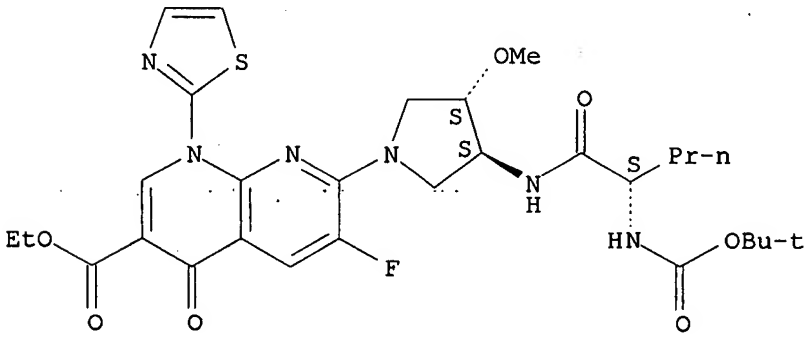
Absolute stereochemistry.



● HCl

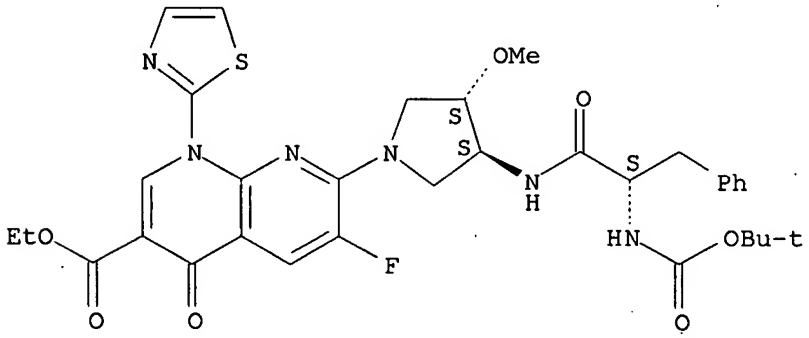
RN 177751-46-1 ZCAPLUS
CN 1,8-Naphthyridine-3-carboxylic acid, 7-[3-[[2-[[(1,1-dimethylethoxy)carbonyl]amino]-1-oxopentyl]amino]-4-methoxy-1-pyrrolidinyl]-6-fluoro-1,4-dihydro-4-oxo-1-(2-thiazolyl)-, ethyl ester, [3S-[3α(R*),4β]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



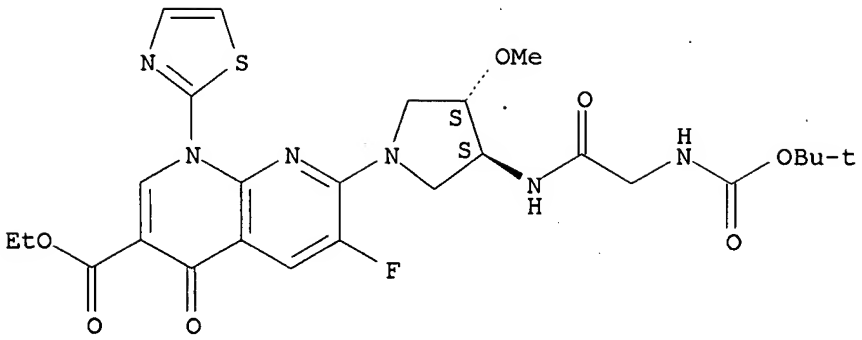
RN 177751-47-2 ZCAPLUS
CN 1,8-Naphthyridine-3-carboxylic acid, 7-[3-[[2-[[(1,1-dimethylethoxy)carbonyl]amino]-1-oxo-3-phenylpropyl]amino]-4-methoxy-1-pyrrolidinyl]-6-fluoro-1,4-dihydro-4-oxo-1-(2-thiazolyl)-, ethyl ester, [3S-[3α(R*),4β]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



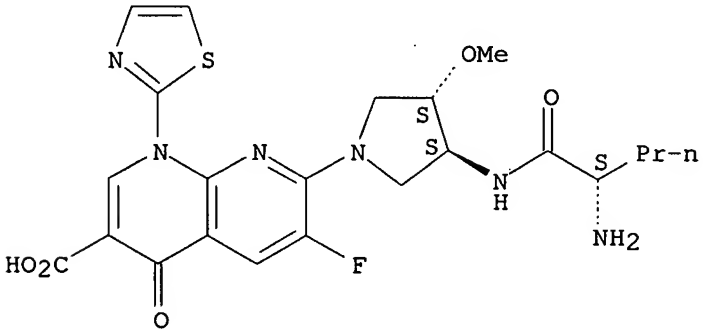
RN 177751-48-3 ZCAPLUS
CN 1,8-Naphthyridine-3-carboxylic acid, 7-[3-[[[[(1,1-dimethylethoxy)carbonyl]amino]acetyl]amino]-4-methoxy-1-pyrrolidinyl]-6-fluoro-1,4-dihydro-4-oxo-1-(2-thiazolyl)-, ethyl ester, (3S-trans)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 177751-56-3 ZCAPLUS
CN 1,8-Naphthyridine-3-carboxylic acid, 7-[3-[(2-amino-1-oxopentyl)amino]-4-methoxy-1-pyrrolidinyl]-6-fluoro-1,4-dihydro-4-oxo-1-(2-thiazolyl)-, monohydrochloride, [3S-[3α(R*),4β]]- (9CI) (CA INDEX NAME)

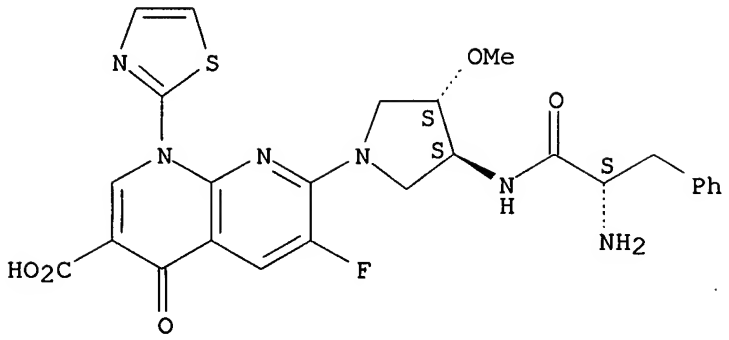
Absolute stereochemistry.



● HCl

RN 177751-57-4 ZCAPLUS
CN 1,8-Naphthyridine-3-carboxylic acid, 7-[3-[(2-amino-1-oxo-3-phenylpropyl)amino]-4-methoxy-1-pyrrolidinyl]-6-fluoro-1,4-dihydro-4-oxo-1-(2-thiazolyl)-, monohydrochloride, [3S-[3α(R*),4β]]- (9CI) (CA INDEX NAME)

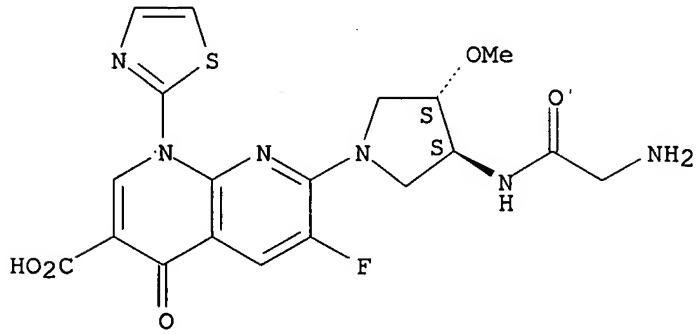
Absolute stereochemistry.



● HCl

RN 177751-65-4 ZCAPLUS
CN 1,8-Naphthyridine-3-carboxylic acid, 7-[3-[(aminoacetyl)amino]-4-methoxy-1-pyrrolidinyl]-6-fluoro-1,4-dihydro-4-oxo-1-(2-thiazolyl)-, monohydrochloride, (3S-trans)- (9CI) (CA INDEX NAME)

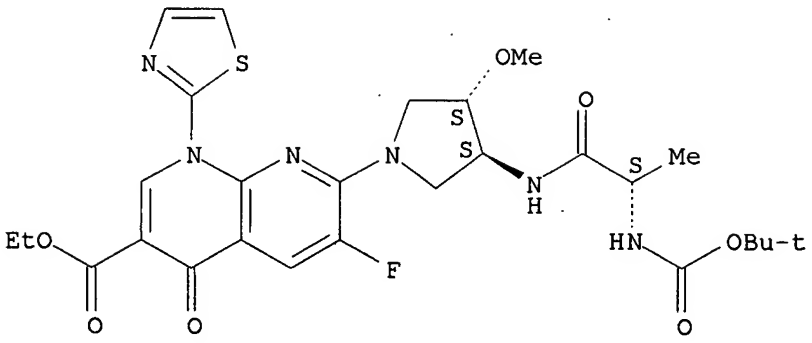
Absolute stereochemistry.



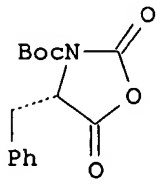
● HCl

IT 177751-69-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of naphthyridines as antitumor agents)
RN 177751-69-8 ZCAPLUS
CN 1,8-Naphthyridine-3-carboxylic acid, 7-[3-[[2-[[(1,1-dimethylethoxy)carbonyl]amino]-1-oxopropyl]amino]-4-methoxy-1-pyrrolidinyl]-6-fluoro-1,4-dihydro-4-oxo-1-(2-thiazolyl)-, ethyl ester, [3S-[3α(R*),4β]]- (9CI) (CA INDEX NAME)

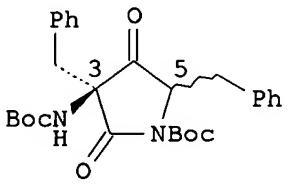
Absolute stereochemistry.



L4 ANSWER 73 OF 76 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:13593 ZCAPLUS
DOCUMENT NUMBER: 124:202990
TITLE: Base-Induced Dimerization of Urethane-Protected Amino Acid N-Carboxanhydrides
AUTHOR(S): Leban, Johann J.; Colson, Kimberly L.
CORPORATE SOURCE: Divisions of Organic Chemistry and Bioanalytical Sciences, Wellcome Research Laboratories, Research Triangle Park, NC, 27709, USA
SOURCE: Journal of Organic Chemistry (1996), 61(1), 228-31
CODEN: JOCEAH; ISSN: 0022-3263
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 124:202990
GI



I



II

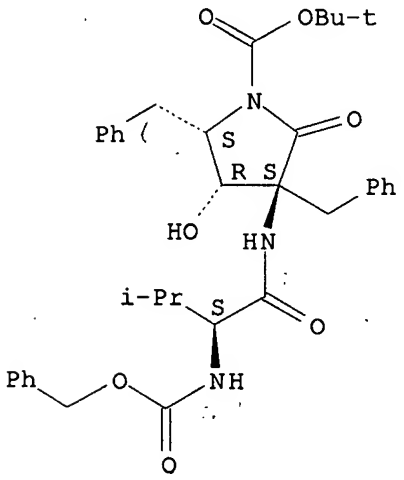
AB Tert-Butoxycarbonyl (Boc)-protected phenylalanine N-carboxyanhydride (I) dimerizes in the presence of base in aprotic media to form cis- and trans-3,5-dibenzyl-2,4-dioxo-1-pyrrolidines II. Depending on the nature of the base, different ratios of isomers were obtained. The reaction with LiNn(SiMe3)2 lead to one isomer only. After deprotection of the Boc groups and coupling of Z-Val-OH, a homogeneous product was obtained. Reduction with NaBH4 again gave a homogeneous product. NOE spectroscopy and x-ray crystallog. identified the stereochem. in positions 3 and 5 of the pyrrolidine as cis. When DBU was used as the base, the condensation led to a 1:3 ratio of isomers. The major isomer was different from the one obtained with LiN(SiMe3)2. The Z-Val derivative from this compound was obtained as a 1:1 mixture of isomers, leading to the conclusion that this condensation product was an enantiomeric mixture of trans isomers. The pure cis isomer from the LiN(SiMe3)2 reaction was converted to a mixture of cis and trans isomers in a ratio of 1:3 when treated with DBU. The Z-Val derivative of the trans isomer from this conversion was again a 1:1 mixture; therefore, the cis isomer obtained with LiN(SiMe3)2 is believed to be an

enantiomeric mixture Several other examples indicated that this reaction occurred also with other tert-butoxycarbonyl-protected N-carboxyanhydrides.

IT 174149-94-1P 174291-20-4P
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(base-induced dimerization of urethane-protected amino acid carboxaynhydrides to amino(dialkyl)pyrrolidinediones)

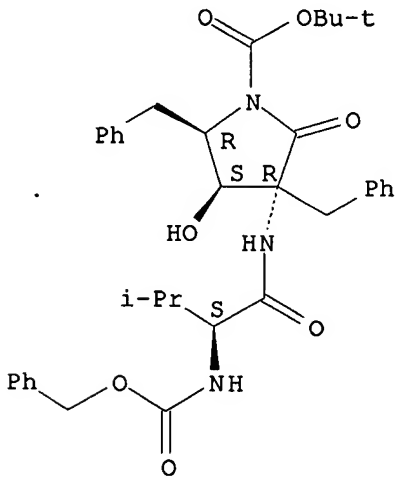
RN 174149-94-1 ZCAPLUS
CN 1-Pyrrolidinecarboxylic acid, 4-hydroxy-3-[[3-methyl-1-oxo-2-[[(phenylmethoxy)carbonyl]amino]butyl]amino]-2-oxo-3,5-bis(phenylmethyl)-, 1,1-dimethylethyl ester, [3S-[3α(R*),4β,5β]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



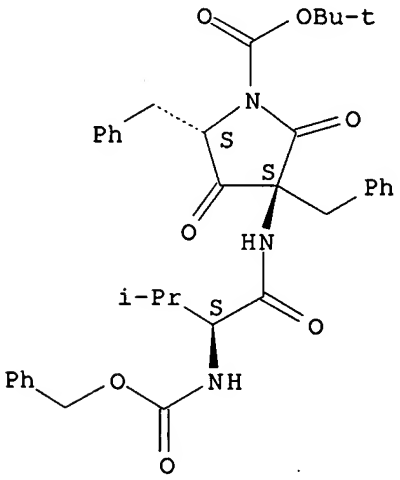
RN 174291-20-4 ZCAPLUS
CN 1-Pyrrolidinecarboxylic acid, 4-hydroxy-3-[[3-methyl-1-oxo-2-[[(phenylmethoxy)carbonyl]amino]butyl]amino]-2-oxo-3,5-bis(phenylmethyl)-, 1,1-dimethylethyl ester, [3R-[3α(S*),4β,5β]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



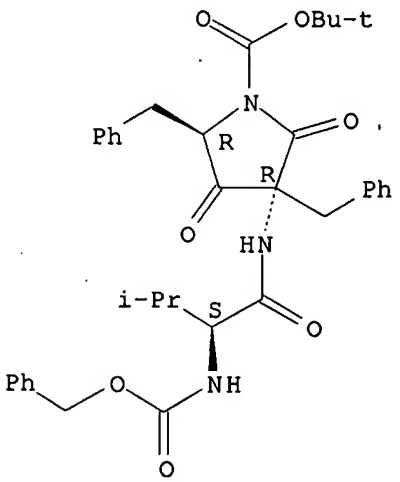
IT 174149-93-0P 174291-19-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(base-induced dimerization of urethane-protected amino acid carboxaynhydrides to amino(dialkyl)pyrrolidinediones)
RN 174149-93-0 ZCAPLUS
CN 1-Pyrrolidinecarboxylic acid, 3-[[3-methyl-1-oxo-2-[[(phenylmethoxy)carbonyl]amino]butyl]amino]-2,4-dioxo-3,5-bis(phenylmethyl)-, 1,1-dimethylethyl ester, [3S-[3α(R*),5β]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 174291-19-1 ZCAPLUS
CN 1-Pyrrolidinecarboxylic acid, 3-[[3-methyl-1-oxo-2-[[(phenylmethoxy)carbonyl]amino]butyl]amino]-2,4-dioxo-3,5-bis(phenylmethyl)-, 1,1-dimethylethyl ester, [3R-[3α(S*),5β]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

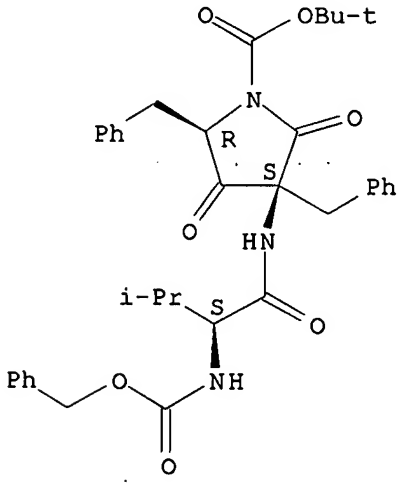


IT 174291-21-5P 174291-22-6P
RL: SPN (Synthetic preparation); PREP (Preparation)

(base-induced dimerization of urethane-protected amino acid carboxaynhydrides to amino(dialkyl)pyrrolidinediones)

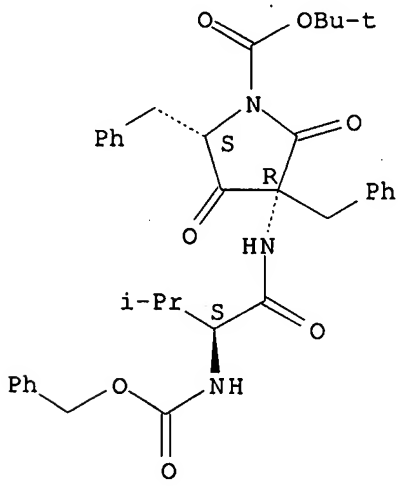
RN 174291-21-5 ZCAPLUS
CN 1-Pyrrolidinecarboxylic acid, 3-[[3-methyl-1-oxo-2-[[(phenylmethoxy)carbonyl]amino]butyl]amino]-2,4-dioxo-3,5-bis(phenylmethyl)-, 1,1-dimethylethyl ester, [3S-[3α(R*),5α]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 174291-22-6 ZCAPLUS
CN 1-Pyrrolidinecarboxylic acid, 3-[[3-methyl-1-oxo-2-[[(phenylmethoxy)carbonyl]amino]butyl]amino]-2,4-dioxo-3,5-bis(phenylmethyl)-, 1,1-dimethylethyl ester, [3R-[3α(S*),5α]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 74 OF 76 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1993:650376 ZCAPLUS
DOCUMENT NUMBER: 119:250376
TITLE: Preparation of 2- and 3- amino and azido derivatives

of 1,5-iminosugars

INVENTOR(S): Khanna, Ish K.; Mueller, Richard A.; Weier, Richard M.; Stealey, Michael A.

PATENT ASSIGNEE(S): G.D. Searle and Co., USA

SOURCE: U.S., 20 pp.
CODEN: USXXAM

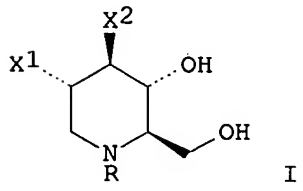
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5216168	A	19930601	US 1992-861686	19920401
US 5270468	A	19931214	US 1993-1953	19930108
CA 2093076	A1	19931002	CA 1993-2093076	19930331
CA 2093076	C	20050104		
EP 566557	A1	19931020	EP 1993-870061	19930331
EP 566557	B1	19960904		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 06016632	A	19940125	JP 1993-109731	19930331
JP 3209612	B2	20010917		
AT 142201	T	19960915	AT 1993-870061	19930331
ES 2095032	T3	19970201	ES 1993-870061	19930331

PRIORITY APPLN. INFO.: US 1992-861686 A3 19920401
US 1992-861696 A 19920401

OTHER SOURCE(S): MARPAT 119:250376

GI



I

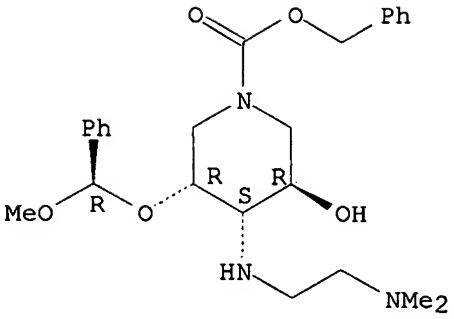
AB Title compds. I (R = H, alkyl, aralkyl; X1 = HO, N3 H2N, R1NH, R2N, R3CONH wherein R1, R2 = alkyl, R3 = H, alkyl; X2 = N3, HO, H2N, and provided further that at least 1 of X1 and X2 is not HO) showing antiviral activity as demonstrated against lentivirus, are prepared 2-Azido-1,2,5-trideoxy-1,5-imino-4,6-O-(R-phenylmethylene-D-glucitol (preparation given) in F3CCO2H/H2O was stirred at 22° for 18 h, the solvent removed under reduced pressure and the residue passed through an ion-exchanged column to give I (R = H, X1 = N3, X2 = HO).

IT 150781-10-5P 150781-12-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, in preparation of virucides)

RN 150781-10-5 ZCAPLUS

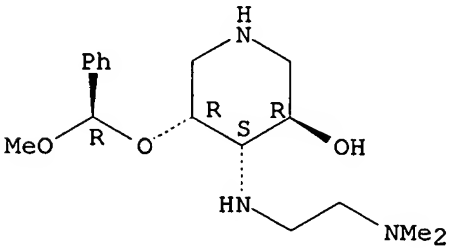
CN 1-Piperidinecarboxylic acid, 4-[[2-(dimethylamino)ethyl]amino]-3-hydroxy-5-(methoxyphenylmethoxy)-, phenylmethyl ester, [3R-[3α,4β,5β(R*)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



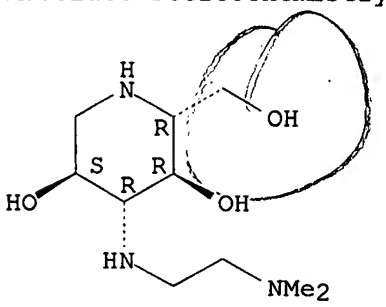
RN 150781-12-7 ZCAPLUS
CN 3-Piperidinol, 4-[[2-(dimethylamino)ethyl]amino]-5-(methoxyphenylmethoxy)-, [3R-[3α,4β,5β(R*)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 150781-13-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of, as virucide)
RN 150781-13-8 ZCAPLUS
CN 3,5-Piperidinediol, 4-[[2-(dimethylamino)ethyl]amino]-2-(hydroxymethyl)-, [2R-(2α,3β,4α,5β)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 75 OF 76 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1993:581151 ZCAPLUS
DOCUMENT NUMBER: 119:181151
TITLE: Preparation of 2- and 3-amino and -azido derivatives of 1,5-iminosugars
INVENTOR(S): Khanna, Ish K.; Mueller, Richard A.; Weier, Richard M.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA
SOURCE: U.S., 22 pp.

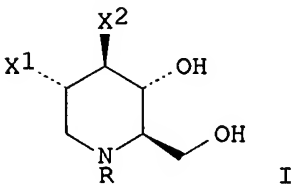
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5206251	A	19930427	US 1992-861696	19920401
US 5268482	A	19931207	US 1992-942572	19920909
US 5334717	A	19940802	US 1993-2380	19930108
CA 2093077	A1	19931002	CA 1993-2093077	19930331
CA 2093077	C	20050222		
EP 566557	A1	19931020	EP 1993-870061	19930331
EP 566557	B1	19960904		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 06016631	A	19940125	JP 1993-109730	19930331
JP 3208221	B2	20010910		
AT 142201	T	19960915	AT 1993-870061	19930331
ES 2095032	T3	19970201	ES 1993-870061	19930331
JP 2001348386	A	20011218	JP 2001-106995	19930331
JP 3520269	B2	20040419		
US 5331096	A	19940719	US 1993-100850	19930802
US 5342951	A	19940830	US 1993-100788	19930802
US 5391746	A	19950221	US 1993-169233	19931220
US 5436341	A	19950725	US 1994-323706	19941017
US 5550243	A	19960827	US 1995-398827	19950306

PRIORITY APPLN. INFO.:
US 1992-861686 A 19920401
US 1992-861696 A2 19920401
US 1992-942572 A3 19920909
US 1993-2380 A3 19930108
JP 1993-109730 A3 19930331
US 1993-169233 A3 19931220
US 1994-323706 A3 19941017

OTHER SOURCE(S): CASREACT 119:181151; MARPAT 119:181151

GI



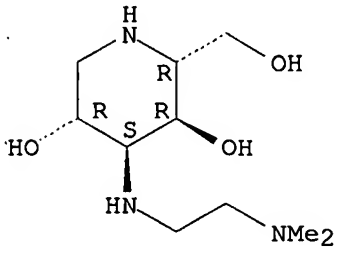
I

AB Title compds., derivs. of 1-deoxynojirimycin I (R = H, alkyl, F3C(CH2)3, X1 = N3, HO, H2N; X2 = HO, H2N) useful as inhibitors of lentiviruses, are prepared I showed inhibition of visna virus in vitro in a plaque reduction assay or for inhibition of HIV-1. 2-Azido-1,2,5-trideoxy-1,5-imino-4,6-O-(R-phenylmethylene)-D-glucitol (preparation given) in MeOH was added to mol. sieves, followed by Et2CHCHO, AcOH and NaBH3CN to give the 1,5-(2-ethylbutyl)imino derivative which was heated with F3CCO2H to give I (R = H, X1 = N3, X2 = HO).

IT 150271-58-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of, as virucide)

RN 150271-58-2 ZCAPLUS
CN 3,5-Piperidinediol, 4-[[2-(dimethylamino)ethyl]amino]-2-(hydroxymethyl)-, [2R-(2α,3β,4β,5α)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



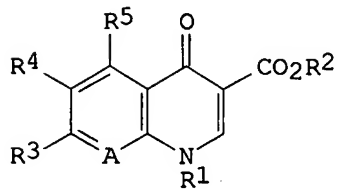
L4 ANSWER 76 OF 76 ZCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1990:497462 ZCAPLUS
DOCUMENT NUMBER: 113:97462
TITLE: Preparation of 7-pyrrolidino-3-quinolone- and -naphthyridonecarboxylates, substituted (oxa)diazabicyclooctane and -nonane intermediates for their preparation, and their use as bactericides and feed additives
INVENTOR(S): Petersen, Uwe; Schenke, Thomas; Krebs, Andreas; Grohe, Klaus; Schriewer, Michael; Haller, Ingo; Metzger, Karl Georg; Endermann, Rainer; Zeiler, Hans Joachim
PATENT ASSIGNEE(S): Bayer A.-G., Germany
SOURCE: Ger. Offen., 74 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3906365	A1	19900118	DE 1989-3906365	19890301
AU 8936594	A	19900315	AU 1989-36594	19890619
AU 616277	B2	19911024		
NO 8902715	A	19900116	NO 1989-2715	19890629
NO 168889	B	19920106		
NO 168889	C	19920415		
EP 350733	A2	19900117	EP 1989-111950	19890630
EP 350733	A3	19901227		
EP 350733	B1	19960313		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
CN 1039589	A	19900214	CN 1989-104574	19890630
CN 1027165	B	19941228		
US 4990517	A	19910205	US 1989-375434	19890630
AT 135354	T	19960315	AT 1989-111950	19890630
EP 757990	A1	19970212	EP 1996-113744	19890630
EP 757990	B1	20050330		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
ES 2109219	T3	19980116	ES 1989-111950	19890630
AT 292127	T	20050415	AT 1996-113744	19890630
ES 2240984	T3	20051016	ES 1996-113744	19890630
JP 02069474	A	19900308	JP 1989-178218	19890712
JP 2771853	B2	19980702		

IL 90940	A	19940412	IL 1989-90940		19890712
FI 8903403	A	19900116	FI 1989-3403		19890713
FI 94251	B	19950428			
FI 94251	C	19950810			
DD 285601	A5	19901219	DD 1989-330777		19890713
CA 1340114	C	19981103	CA 1989-605572		19890713
DK 8903500	A	19900116	DK 1989-3500		19890714
DK 170404	B1	19950821			
ZA 8905366	A	19900425	ZA 1989-5366		19890714
HU 52087	A2	19900628	HU 1989-3578		19890714
HU 208130	B	19930830			
HU 65936	A2	19940829	HU 1993-1002		19890714
HU 213099	B	19970228			
US 5059597	A	19911022	US 1990-580906		19900910
US 5416096	A	19950516	US 1991-737631		19910730
AU 9210283	A	19920227	AU 1992-10283		19920116
AU 650316	B2	19940616			
AU 9225286	A	19921126	AU 1992-25286		19920922
AU 658667	B2	19950427			
CN 1097759	A	19950125	CN 1994-100328		19940121
CN 1036005	B	19971001			
AU 9460556	A	19940609	AU 1994-60556		19940419
AU 668286	B2	19960426			
AU 9460557	A	19940609	AU 1994-60557		19940419
AU 668287	B2	19960426			
AU 9472991	A	19941208	AU 1994-72991		19940915
AU 671386	B2	19960822			
US 5607942	A	19970304	US 1995-406448		19950320
CN 1143080	A	19970219	CN 1996-103664		19960412
KR 156375	B1	19981001	KR 1997-53066		19971016
JP 10182600	A	19980707	JP 1998-13154		19980108
JP 3001848	B2	20000124			
CA 1340553	C	19990518	CA 1998-617094		19980424
PRIORITY APPLN. INFO.:			DE 1988-3824072	A1	19880715
			DE 1989-3906365	A	19890301
			EP 1989-111950	A3	19890630
			US 1989-375434	A3	19890630
			JP 1989-178218	A3	19890712
			CA 1989-605572	A3	19890713
			KR 1989-10217	A3	19890715
			US 1990-580906	A3	19900910
			US 1991-737631	A3	19910730

OTHER SOURCE(S): MARPAT 113:97462

GI



I

AB The title compds. I [R1 = C1-4 alkyl, C2-4 alkenyl, C3-6 cycloalkyl, 2-hydroxyethyl, 2-fluoroethyl, MeO, NH2, MeNH, EtNH, Me2N, or Ph with ≥1 F; R2 = H, C1-4 alkyl, or (5-methyl-2-oxo-1,3-dioxol-4-yl)methyl; R3 = a pyrrolidinyl-based heterocycle; R4 = halogen; R5 = H, NH2, C1-4 alkylamino C1-3 dialkylamino, OH, C1-4 alkoxy, HS, C1-4 alkylthio,